

=> d his full

(FILE 'HOME' ENTERED AT 08:11:55 ON 27 JUN 2005)  
DEL GITLIPR/A

FILE 'REGISTRY' ENTERED AT 08:12:51 ON 27 JUN 2005

L1 STR  
L2 STR L1  
L3 12 SEA SSS SAM L2  
DEL QAZ122F0/A  
L4 224 SEA SSS FUL L2  
SAV TEM QAZ122C1/A L4  
L5 STR L2  
L6 0 SEA SUB=L4 SSS SAM L5  
L7 13 SEA SUB=L4 SSS FUL L5  
ACT QAZ122C12PR/A

-----  
L8 STR  
L9 ( 13409) SEA CSS FUL L8  
L10 STR  
L11 20 SEA SUB=L9 SSS FUL L10  
-----  
L12 STR L5  
L13 1 SEA SUB=L4 SSS SAM L12  
D SCA  
L14 19 SEA SUB=L4 SSS FUL L12  
SAV TEM QAZIC12R/A L14

FILE 'HCAPLUS' ENTERED AT 08:22:00 ON 27 JUN 2005

L15 12 SEA ABB=ON PLU=ON L7  
L16 1 SEA ABB=ON PLU=ON L14 AND L11  
E VAN RHEENEN V/AU  
L17 31 SEA ABB=ON PLU=ON ("VAN RHEENEN V"/AU OR "VAN RHEENEN  
VERLAN"/AU OR "VAN RHEENEN VERLAN H"/AU OR "VAN RHEENEN VERLAN  
HENRY"/AU OR "VAN RHEENEN VERLAND HENRY"/AU)  
E HESSLER E/AU  
L18 22 SEA ABB=ON PLU=ON ("HESSLER ED"/AU OR "HESSLER ED J"/AU OR  
"HESSLER EDWARD"/AU OR "HESSLER EDWARD J"/AU OR "HESSLER  
EDWARD JAMES"/AU)  
L19 2 SEA ABB=ON PLU=ON (BRID? (1A)ORG?)/CS,PA

FILE 'HCAOLD' ENTERED AT 08:23:44 ON 27 JUN 2005

L20 3 SEA ABB=ON PLU=ON L7  
SEL AN  
EDIT E1-E3 /AN /OREF

FILE 'HCAPLUS' ENTERED AT 08:24:11 ON 27 JUN 2005

L21 6 SEA ABB=ON PLU=ON ("CA59:8825E"/OREF OR "CA62:621C"/OREF OR  
"CA63:655G"/OREF)  
L22 1 SEA ABB=ON PLU=ON (L15 OR L21) AND (L17 OR L18 OR L19)  
L23 15 SEA ABB=ON PLU=ON (L15 OR L21) NOT L22  
L24 QUE ABB=ON PLU=ON PY<+2001 OR AY<=2001 OR PRY<=2001 OR  
PD<20010608 OR AD<20010608 OR PRD<20010608  
L25 15 SEA ABB=ON PLU=ON L23 AND L24  
L26 1 SEA ABB=ON PLU=ON L16 AND (L17 OR L18 OR L19)  
L27 1 SEA ABB=ON PLU=ON L22 OR L26

FILE 'HCAOLD' ENTERED AT 08:27:47 ON 27 JUN 2005

SEL HIT RN L20

FILE 'REGISTRY' ENTERED AT 08:27:56 ON 27 JUN 2005

L28 4 SEA ABB=ON PLU=ON (102490-33-5/RN OR 1624-60-8/RN OR  
1103-94-2/RN OR 1249-41-8/RN)

=> b reg

FILE 'REGISTRY' ENTERED AT 08:28:18 ON 27 JUN 2005

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Property values tagged with IC are from the ZIC/VINITI data file  
 provided by InfoChem.

STRUCTURE FILE UPDATES: 26 JUN 2005 HIGHEST RN 852987-17-8  
 DICTIONARY FILE UPDATES: 26 JUN 2005 HIGHEST RN 852987-17-8

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TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when  
 conducting SmartSELECT searches.

\*\*\*\*\*  
 \*  
 \* The CA roles and document type information have been removed from \*  
 \* the IDE default display format and the ED field has been added, \*  
 \* effective March 20, 2005. A new display format, IDERL, is now \*  
 \* available and contains the CA role and document type information. \*  
 \*  
 \*\*\*\*\*

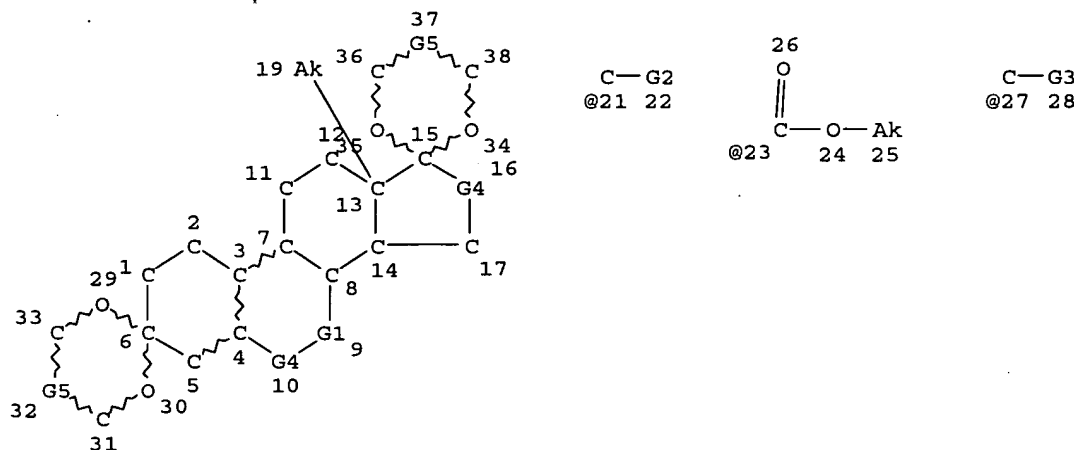
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more  
 information enter HELP PROP at an arrow prompt in the file or refer  
 to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d que sta l7.

L2

STR



VAR G1=C/21  
 VAR G2=AK/23  
 VAR G3=AK/OH/X  
 VAR G4=C/27  
 REP G5=(0-1) C  
 NODE ATTRIBUTES:  
 DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
 RING(S) ARE ISOLATED OR EMBEDDED

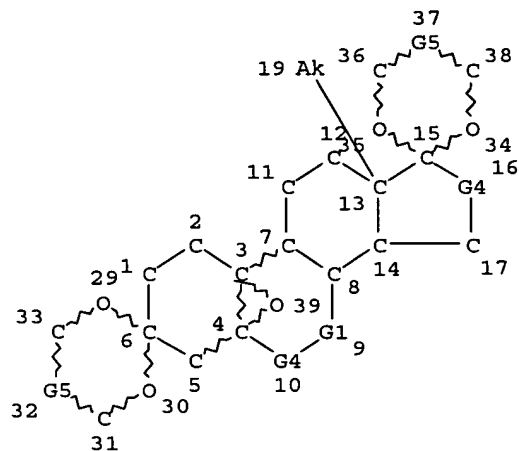
Search done by Noble Jarrell

NUMBER OF NODES IS 36

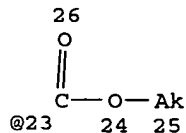
STEREO ATTRIBUTES: NONE

L4 224 SEA FILE=REGISTRY SSS FUL L2

L5 STR



C—G2  
@21 22



C—G3  
@27 28

VAR G1=C/21

VAR G2=AK/23

VAR G3=AK/OH/X

VAR G4=C/27

REP G5=(0-1) C

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 37

STEREO ATTRIBUTES: NONE

L7 13 SEA FILE=REGISTRY SUB=L4 SSS FUL L5

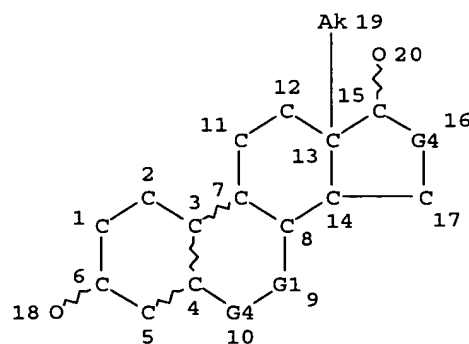
100.0% PROCESSED 37 ITERATIONS

13 ANSWERS

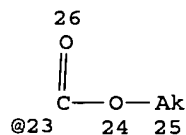
SEARCH TIME: 00.00.01

=> d que sta l11

L8 STR



C—G2  
@21 22



C—G3  
@27 28

VAR G1=C/21

VAR G2=AK/23

Search done by Noble Jarrell

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VAR G3=AK/OH/X
VAR G4=C/27
NODE ATTRIBUTES:
CONNECT IS M1 RC AT 3
CONNECT IS M1 RC AT 4
CONNECT IS M1 RC AT 6
CONNECT IS M1 RC AT 15
CONNECT IS M1 RC AT 18
CONNECT IS M1 RC AT 20
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

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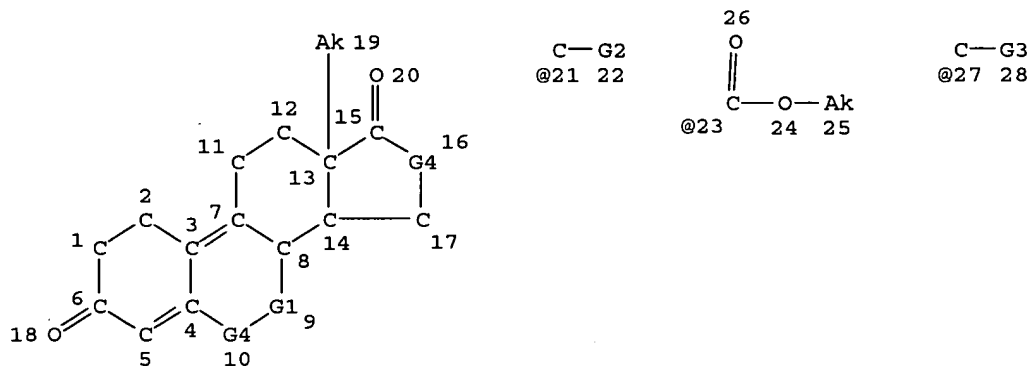
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 28

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STEREO ATTRIBUTES: NONE
L9 ( 13409)SEA FILE=REGISTRY CSS FUL L8
L10 STR

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VAR G1=C/21
VAR G2=AK/23
VAR G3=AK/OH/X
VAR G4=C/27
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 28

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STEREO ATTRIBUTES: NONE
L11 20 SEA FILE=REGISTRY SUB=L9 SSS FUL L10

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100.0% PROCESSED 24 ITERATIONS
SEARCH TIME: 00.00.01

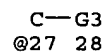
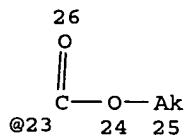
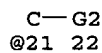
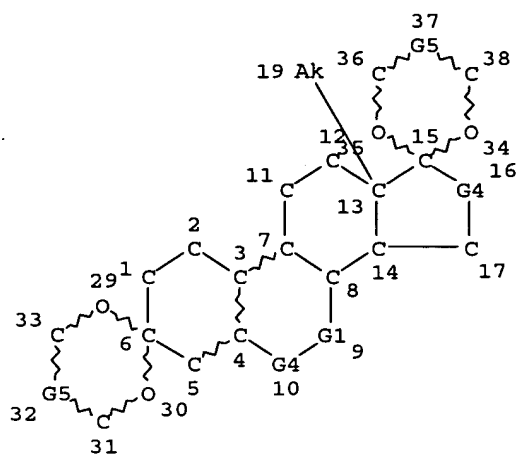
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20 ANSWERS

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=> d que sta l14
L2 STR

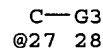
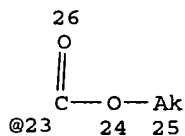
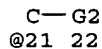
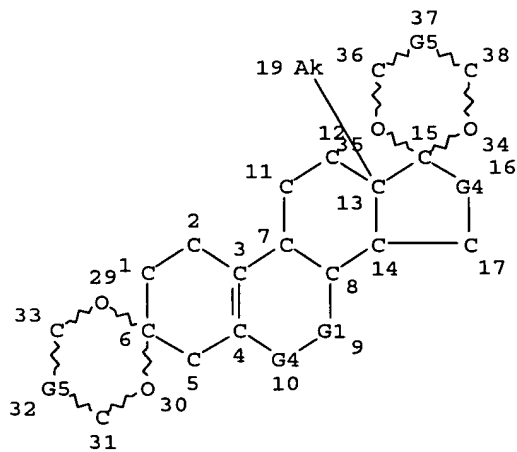
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VAR G1=C/21  
 VAR G2=AK/23  
 VAR G3=AK/OH/X  
 VAR G4=C/27  
 REP G5=(0-1) C  
 NODE ATTRIBUTES:  
 DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
 RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 36

STEREO ATTRIBUTES: NONE  
 L4 224 SEA FILE=REGISTRY SSS FUL L2  
 L12 STR



VAR G1=C/21  
 VAR G2=AK/23  
 VAR G3=AK/OH/X  
 VAR G4=C/27  
 REP G5=(0-1) C  
 NODE ATTRIBUTES:  
 DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 36

STEREO ATTRIBUTES: NONE  
L14 19 SEA FILE=REGISTRY SUB=L4 SSS FUL L12

100.0% PROCESSED 52 ITERATIONS ( 1 INCOMPLETE) 19 ANSWERS  
SEARCH TIME: 00.00.01

=> b hcap  
FILE 'HCAPLUS' ENTERED AT 08:28:32 ON 27 JUN 2005  
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FILE COVERS 1907 - 27 Jun 2005 VOL 143 ISS 1  
FILE LAST UPDATED: 26 Jun 2005 (20050626/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all fhitr 127 tot

L27 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN  
AN 2002:964483 HCAPLUS  
DN 138:24878  
ED Entered STN: 20 Dec 2002  
TI Process for preparing estra-4,9(10)-diene-3,17-dione steroids from 19-nor-androst-4-ene-3-one steroids  
IN Van Rhee, Verlan H.; Hessler, Edward J.  
PA Bridge Organics Co., USA  
SO PCT Int. Appl., 23 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
IC ICM C12N  
CC 32-3 (Steroids)  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002101014	A2	20021219	WO 2002-US18305	20020607
	WO 2002101014	A3	20040325		
	WO 2002101014	B1	20040506		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,				

Search done by Noble Jarrell

KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,  
GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,  
GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003004333	A1	20030102	US 2002-163727	20020606
US 6812358	B2	20041102		
US 2004087785	A1	20040506	US 2003-695122	20031028
PRAI US 2001-296999P	P	20010608		
US 2002-163727	A	20020606		

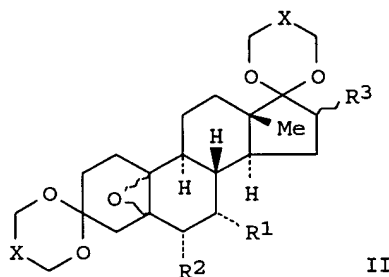
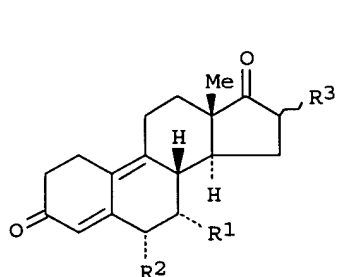
## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
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WO 2002101014	ICM	C12N
WO 2002101014	ECLA	C07J001/00C2; C07J071/00B1
US 2003004333	NCL	552/623.000; 540/543.000
	ECLA	C07J001/00C2; C07J071/00B1
US 2004087785	NCL	540/008.000; 540/076.000
	ECLA	C07J001/00C2; C07J071/00B1

OS CASREACT 138:24878; MARPAT 138:24878

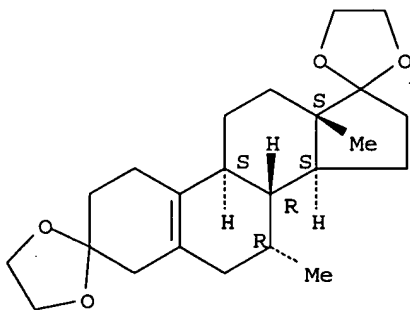
GI



- AB The present invention discloses a novel process for preparing  
estra-4,9(10)-diene-3,17-dione derivs. such as I [R1 = Me, H, CO2Me; R2 =  
Me, F, H; R3 = Me, OH, F, H], from readily available 19-nor-androst-4-ene-  
3-one derivs. such as II [X = bond, C(Me)2, CH2], by a three-step process.  
Thus, epoxidn. of 7 $\alpha$ -methyl-estra-5(10)-ene-3,17-dione-3,17-bis-  
ethylene glycol ketal afforded 7 $\alpha$ -methyl-estra-5(10)-oxido-3,17-  
dione-3,17-bis-ethylene glycol ketal which upon treatment with  
hydrochloric acid provided 10-hydroxy-7 $\alpha$ -methyl-estra-4-ene-3,17-  
dione (III) and 5,10-dihydroxy-7 $\alpha$ -methyl-estra-4-ene-3,17-dione  
(IV). III and IV were reacted with concentrated sulfuric acid to afford  
estra-4,9(10)-diene-3,17-dione I [R1 = Me; R2, R3 = H]. Products of this  
process are important intermediates in the preparation of biol. active  
substances.
- ST estradienedione steroid prepn norandrosteneone epoxidn; oxidoestradiene  
dihydroxyestraenedione hydroxyestraenedione prepn
- IT Ketals  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(estra-5(10)-ene-3,17-dione-3,17-bis-ketal derivative; in preparation of  
estra-4,9(10)-diene steroid derivs.)
- IT Acids, reactions  
RL: RGT (Reagent); RACT (Reactant or reagent)  
(inorg.; in preparation of estradiene steroids from  
10-hydroxy-estra-4-ene-3,17-dione and 5,10-dihydroxy-estra-4-ene-3,17-  
dione steroids)
- IT Epoxidation  
(of estradiene-5(10)-ene-3,17-dione-3,17-bis-glycol ketal in preparation of  
estra-5(10)-oxido-3,17-dione-3,17-bis-glycol ketal)
- IT Estrogens  
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP  
(Preparation)  
(preparation of estradiene steroids from 19-nor-androst-4-ene-3-one

steroids)  
 IT 19-Norsteroids  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of estra-4,9(10)-diene steroids from 19-nor-androst-4-ene-3-one steroids)  
 IT 13209-45-5P, Estra-4,6-diene-3,17-dione 478156-84-2P  
 478156-85-3P 478156-86-4P 478156-87-5P 478156-88-6P  
 478156-89-7P 478156-91-1P 478156-93-3P 478156-94-4P  
 478156-96-6P 478242-79-4P  
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of estra-4,9(10)-diene steroids from 19-nor-androst-4-ene-3-one steroids)  
 IT 5173-46-6P, Estra-4,9-diene-3,17-dione 24130-12-9P  
 30164-84-2P 478156-90-0P 478156-92-2P  
 478156-97-7P  
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of estra-4,9(10)-diene steroids from 19-nor-androst-4-ene-3-one steroids)  
 IT 734-32-7, 19-Nor-androst-4-ene-3,17-dione 2220-74-8 2503-06-2,  
 Estra-5(10),9(11)-diene-3,17-dione 17000-78-1 33585-96-5  
 139444-50-1 478156-95-5  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of estra-4,9(10)-diene steroids from 19-nor-androst-4-ene-3-one steroids)  
 IT 79-21-0, Peracetic acid 937-14-4, m-Chloroperbenzoic acid 7664-38-2,  
 Phosphoric acid, reactions 7664-93-9, Sulfuric acid, reactions  
 RL: RGT (Reagent); RACT (Reactant or reagent)  
 (preparation of estra-4,9(10)-diene steroids from 19-nor-androst-4-ene-3-one steroids)  
 IT 478156-84-2P  
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of estra-4,9(10)-diene steroids from 19-nor-androst-4-ene-3-one steroids)  
 RN 478156-84-2 HCAPLUS  
 CN Estr-5(10)-ene-3,17-dione, 7-methyl-, cyclic bis(1,2-ethanediyl acetal),  
 (7 $\alpha$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d all hitstr 125 tot

L25 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1996:31798 HCAPLUS  
 DN 124:87466  
 ED Entered STN: 17 Jan 1996  
 TI Structure-Activity Relationships of a New Family of Steroidal Aromatase Inhibitors. 1. Synthesis and Evaluation of a Series of Analogs Related to

Search done by Noble Jarrell



19-[(Methylthio)methyl]androstenedione (RU54115)

AU Lesuisse, Dominique; Gourvest, Jean-Francois; Benslimane, Ouafae; Canu, Frank; Delaisi, Christine; Doucet, Bernard; Hartmann, Catherine; Lefrancois, Jean-Michel; Tric, Bernadette; et al.

CS Centre de Recherche, Roussel Uclaf, Romainville, 93230, Fr.

SO Journal of Medicinal Chemistry (1996), 39(3), 757-72  
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

CC 32-4 (Steroids)

Section cross-reference(s): 1, 7

AB During the course of a study aimed at the search for new potent aromatase inhibitors, several new androstenedione analogs were synthesized and evaluated. This study led to the discovery of 19-[(methylthio)methyl]androsta-4,9(11)-diene-3,17-dione (RU54115). The object of the present series of papers is to disclose the result of the structure-activity relationship studies that gave rise to this compound. This first part deals mainly with the substitution in the 19-position of the steroid nucleus. Several parameters were varied, the length of the chain and its rigidity and branching, as well as the nature of the heteroatom itself and its substitution. The interaction of these new compds. with human placental aromatase in competition with the substrate androstenedione was studied by difference visible spectroscopy. The in vivo aromatase-inhibiting activities were evaluated by measuring the estradiol lowering after oral administration of the compds. to PMSG-primed female rats.

ST steroidal aromatase inhibitor methylthiomethylandrostenedione structure activity; androstenedione methylthiomethyl steroidal aromatase inhibitor

IT Molecular structure-biological activity relationship  
(testosterone A-ring reductase-inhibiting, synthesis steroidal aromatase inhibitor structure-activity relationships of 19-[(methylthio)methyl]androstenedione analogs)

IT 137437-39-9P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
(synthesis steroidal aromatase inhibitor structure-activity relationships of 19-[(methylthio)methyl]androstenedione analogs)

IT 137437-16-2P 137437-17-3P 137437-20-8P 137437-26-4P 137437-32-2P  
137437-33-3P 137437-36-6P 137437-37-7P 137437-40-2P 137437-43-5P  
137437-45-7P 137437-46-8P 137437-47-9P 137437-48-0P 137437-50-4P  
137437-52-6P 137437-54-8P 137437-64-0P 172427-87-1P 172427-90-6P  
172427-91-7P 172427-92-8P 172427-93-9P 172427-98-4P 172428-00-1P  
172428-02-3P 172428-04-5P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(synthesis steroidal aromatase inhibitor structure-activity relationships of 19-[(methylthio)methyl]androstenedione analogs)

IT 9039-48-9, Aromatase  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(synthesis steroidal aromatase inhibitor structure-activity relationships of 19-[(methylthio)methyl]androstenedione analogs)

IT 528-76-7, 2,4-Dinitrobenzenesulfonyl chloride 1066-54-2,  
(Trimethylsilyl)acetylene 4333-56-6, Bromocyclopropane 55180-24-0  
102490-33-5 135215-65-5 135215-66-6 135215-67-7  
172427-99-5 172428-25-0 172585-98-7  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(synthesis steroidal aromatase inhibitor structure-activity relationships of 19-[(methylthio)methyl]androstenedione analogs)

IT 137437-13-9P 137437-14-0P 137437-15-1P 137437-18-4P 137437-21-9P  
137437-22-0P 137437-24-2P 137437-25-3P 137437-31-1P 137437-35-5P  
172427-88-2P 172427-89-3P 172427-94-0P 172427-96-2P 172427-97-3P  
172428-03-4P 172428-05-6P 172428-06-7P 172428-07-8P 172428-08-9P

172428-09-0P 172428-10-3P 172428-11-4P 172428-12-5P 172428-13-6P  
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 172428-19-2P 172428-20-5P 172428-21-6P 172428-22-7P 172428-23-8P  
 172428-24-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)

(synthesis steroidal aromatase inhibitor structure-activity  
 relationships of 19-[(methylthio)methyl]androstenedione analogs)

IT 99957-76-3P 172427-95-1P 172428-01-2P

RL: SPN (Synthetic preparation); PREP (Preparation)

(synthesis steroidal aromatase inhibitor structure-activity  
 relationships of 19-[(methylthio)methyl]androstenedione analogs)

IT 102490-33-5

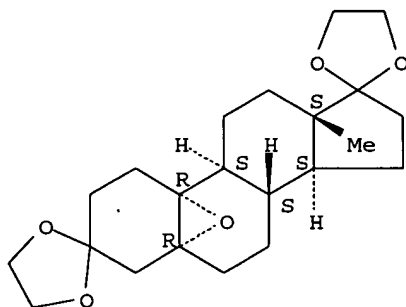
RL: RCT (Reactant); RACT (Reactant or reagent)

(synthesis steroidal aromatase inhibitor structure-activity  
 relationships of 19-[(methylthio)methyl]androstenedione analogs)

RN 102490-33-5 HCAPLUS

CN Estrane-3,17-dione, 5,10-epoxy-, cyclic bis(1,2-ethanediyl acetal),  
 (5 $\alpha$ ,10 $\alpha$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L25 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1992:129377 HCAPLUS

DN 116:129377

ED Entered STN: 03 Apr 1992

TI Process for the preparation of 10-(2-propynyl)estr-4-ene-3,17-dione

IN Whitten, Jeffrey P.; Benson, Harvey D.; Rand, Cynthia L.

PA Merrell Dow Pharmaceuticals, Inc., USA

SO Eur. Pat. Appl., 13 pp.

CODEN: EPXXDW

DT Patent

LA English

IC ICM C07J001-00

ICA C07J021-00; C07J071-00; C07J051-00

CC 32-3 (Steroids)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 459381	A2	19911204	EP 1991-108664	19910528 <--
	EP 459381	A3	19920610		
	EP 459381	B1	19970319		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	CA 2043280	AA	19911201	CA 1991-2043280	19910524 <--
	AU 9177290	A1	19911205	AU 1991-77290	19910524 <--
	AU 649251	B2	19940519		
	ZA 9103963	A	19920429	ZA 1991-3963	19910524 <--
	AT 150465	E	19970415	AT 1991-108664	19910528 <--
	ES 2101702	T3	19970716	ES 1991-108664	19910528 <--
	HU 57791	A2	19911230	HU 1991-1800	19910529 <--
	HU 212575	B	19960829		

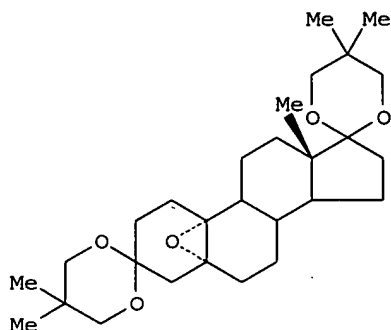
Search done by Noble Jarrell

JP 04235997	A2	19920825	JP 1991-153686	19910530 <--
JP 2989935	B2	19991213		
IL 98384	A1	19950330	IL 1991-98384	19910605 <--
US 5516922	A	19960514	US 1995-468886	19950606 <--
PRAI US 1990-530674	A	19900530	<--	
US 1991-692321	A	19910502	<--	
US 1992-987985	B1	19921209	<--	
US 1993-114802	B1	19930831	<--	
US 1994-359708	B1	19941220	<--	

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
EP 459381	ICM	C07J001-00
	ICA	C07J021-00; C07J071-00; C07J051-00
EP 459381	ECLA	C07J001/00C2; C07J021/00C2; C07J051/00; C07J071/00B1<--
US 5516922	NCL	552/632.000; 552/630.000 <--

GI



III

AB 10-(2-Propynyl)estr-4-ene-3,17-dione (I) was prepared from 19-norandrost-5(10)-ene-3,17-dione (II) in 5 steps via cuprate addition of Me<sub>3</sub>SiC.tplbond.CMe. Thus, II was ketalized with Me<sub>2</sub>C(CH<sub>2</sub>OH)<sub>2</sub>, the ketal was treated with N-bromosuccinimide-MgO, followed by dehydrobromination to give the epoxide III. III was treated with the cuprate prepared from Me<sub>3</sub>SiC.tplbond.CMe, BuLi, and Li methyl-2-thienylcuprate, followed by desilylation and ketal hydrolysis to give I.

ST cuprate addn epoxyandrostane; propynylestrenedione; norandrostenedione propynylation

IT 6224-91-5, 1-Trimethylsilylpropyne  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(cuprate addition reaction of, with epoxyandrostane)

IT 3962-66-1, Estr-5(10)-ene-3,17-dione  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(ketalization of)

IT 139444-50-1P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and bromination-hydroxylation of)

IT 104000-05-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and cuprate addition reaction of)

IT 139444-52-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and deblocking of)

IT 139444-51-2P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and dehydrobromination of)

IT 117626-56-9P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and desilylation of)

IT 77016-85-4P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

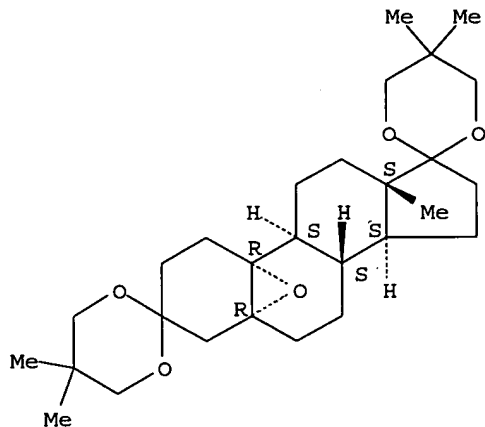
IT 139431-51-9 139522-17-1  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (propynylation by, of epoxyandrostande)

IT 104000-05-7P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and cuprate addition reaction of)

RN 104000-05-7 HCAPLUS

CN Estrane-3,17-dione, 5,10-epoxy-, cyclic bis(2,2-dimethyl-1,3-propanediyl  
 acetal), (5 $\alpha$ ,10 $\alpha$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L25 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1989:95624 HCAPLUS

DN 110:95624

ED Entered STN: 17 Mar 1989

TI Preparation of novel 11-arylestrane and 11-arylpregnane derivatives as  
 antiprogesterins with low or no antiglucocorticoid activity

IN Groen, Marinus Bernard; De Jongh, Hendrik Paul

PA AKZO N. V., Neth.

SO Eur. Pat. Appl., 11 pp.  
 CODEN: EPXXDW

DT Patent

LA English

IC ICM C07J041-00  
 ICS A61K031-565; A61K031-585

CC 32-3 (Steroids)  
 Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 289073	A1	19881102	EP 1988-200689	19880412 <--
	EP 289073	B1	19911127		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, NL, SE				
	AT 69820	E	19911215	AT 1988-200689	19880412 <--
	ES 2045082	T3	19940116	ES 1988-200689	19880412 <--
	ZA 8802643	A	19881130	ZA 1988-2643	19880414 <--
	FI 8801826	A	19881025	FI 1988-1826	19880419 <--

Search done by Noble Jarrell

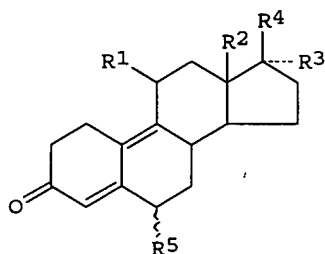
FI 88396	B	19930129		
FI 88396	C	19930510		
US 4871724	A	19891003	US 1988-183851	19880420 <--
CA 1297472	A1	19920317	CA 1988-564606	19880420 <--
DK 8802218	A	19881025	DK 1988-2218	19880422 <--
DK 168294	B1	19940307		
AU 8815072	A1	19881027	AU 1988-15072	19880422 <--
AU 608831	B2	19910418		
JP 63280097	A2	19881117	JP 1988-100010	19880422 <--
CN 88102416	A	19881214	CN 1988-102416	19880423 <--
CN 1019978	B	19930303		
KR 9705318	B1	19970415	KR 1988-4653	19880423 <--
PRAI NL 1987-970	A	19870424	<--	
EP 1988-200689	A	19880412	<--	

## CLASS

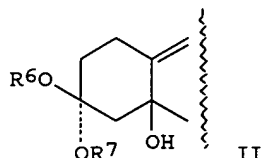
PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
EP 289073	ICM	C07J041-00
	ICS	A61K031-565; A61K031-585
US 4871724	NCL	514/173.000; 514/175.000; 514/181.000; 540/017.000; 540/023.000; 552/594.000; 552/597.000; 552/602.000; 552/605.000; 552/612.000; 552/621.000; 552/644.000; 552/647.000

OS MARPAT 110:95624

GI



I



II

AB The title compds. [I; R1 = aminoaryl; R2 = C1-4 alkyl; R3 = H, OH, substituted (unsatd.) C1-8 hydrocarbyl; R4 = OH, acyloxy, substituted acyl; R3R4 = atoms to complete a ring; R5 = C1-4 hydrocarbyl] useful as antiprogestins (no data) were prepared 5 $\alpha$ ,6 $\alpha$ -Epoxy-11 $\beta$ -hydroxyestrane-3,17-dione-3,17-diethylene acetal (preparation given) was treated with MeMgCl in PhMe/THF and the product was dehydrated with POC13/pyridine to give 6- $\beta$ -methylestra-5(10),9(11)-diene-3,17-dione-3,17-diethylene acetal. The latter was converted in several steps to 11 $\beta$ -[4-(dimethylamino)phenyl]-17 $\beta$ -hydroxy-17 $\alpha$ -(3-hydroxy-1-propynyl)-6 $\beta$ -methylestra-4,9-diene-3-one.

ST estradienone pregnadienone prepn antiprogestin

IT Progestogens

RL: RCT (Reactant); RACT (Reactant or reagent)  
(antagonists, aryloestrane and arylpregnane derivs. as)

IT Contraceptives

(aryloestrane and arylpregnane derivs.)

IT 676-58-4

RL: RCT (Reactant); RACT (Reactant or reagent)  
(Grignard reaction of, with epoxy hydroxyestrane-3,17-dione derivative)

IT 118968-39-1

RL: RCT (Reactant); RACT (Reactant or reagent)  
(cyclization of, in preparation of antiprogestin)

IT 118968-57-3

RL: RCT (Reactant); RACT (Reactant or reagent)  
(dehydration/deketalization of, in preparation of antiprogestin)

IT 59017-03-7

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (epoxidn. of, in preparation of antiprogesterin)

IT 6089-04-9, Propargyl alcohol tetrahydropyranyl ether  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (metalation and condensation of, with estradienedione derivative)

IT 118968-55-1  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (oxidation of)

IT 118968-37-9P 118968-38-0P 118968-39-1P 118968-40-4P 118968-41-5P  
 118968-42-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of, as antiprogesterin)

IT 118968-54-0P 118968-56-2P 118968-58-4P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of, as intermediate for antiprogesterin)

IT 118968-43-7P 118968-44-8P 118968-45-9P 118968-46-0P  
 118968-47-1P 118968-48-2P 118968-49-3P 118968-50-6P 118968-51-7P  
 118968-52-8P 118968-53-9P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of, as intermediate of antiprogesterin)

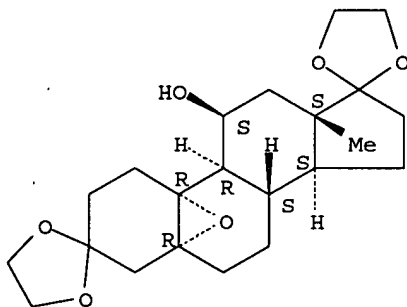
IT 119066-24-9P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of, as progesterin intermediate)

IT 118968-44-8P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of, as intermediate of antiprogesterin)

RN 118968-44-8 HCAPLUS

CN Estrane-3,17-dione, 5,10-epoxy-11-hydroxy-, cyclic bis(1,2-ethanediyl  
 acetal), (5 $\alpha$ ,10 $\alpha$ ,11 $\beta$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L25 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1989:71676 HCAPLUS

DN 110:71676

ED Entered STN: 04 Mar 1989

TI [19-14C]Androstenedione: a new substrate for assaying aromatase and  
 studying its reaction mechanism

AU Covey, Douglas F.; McMullan, Patrick C.; Wixler, Linda L.; Cabell, Mayo  
 CS Sch. Med., Washington Univ., St. Louis, MO, 63110, USA

SO Biochemical and Biophysical Research Communications (1988),  
 157(1), 81-6  
 CODEN: BBRCA9; ISSN: 0006-291X

DT Journal

LA English

CC 7-3 (Enzymes)

Section cross-reference(s): 32

AB [19-14C]androstenedione has been prepared and utilized as a substrate for  
 assaying microsomal human placental aromatase. Enzyme activity is determined  
 by measuring the rate at which [14C]formate is produced by aromatization  
 of this 14C-labeled steroid. Isotope ratio expts. using

Search done by Noble Jarrell

[19-14C]androstenedione and [1 $\beta$ -3H]androstenedione demonstrate that an apparent kinetic H isotope effect exists for the aromatization of the tritiated steroid with  $kH/kT \approx 1.09$ . Metabolic switching occurs to a minor extent ( $\approx 3\%$ ) during aromatization of [1 $\beta$ -3H]androstenedione, but not during the aromatization of [19-14C]androstenedione.

ST androstenedione aromatase

IT Isotope effect

(in aromatization of androstenedione, by aromatase of human placenta, of carbon-14 and tritium)

IT 13864-55-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(aromatization of, by aromatase of human placenta, reaction mechanism in relation to)

IT 9039-48-9, Aromatase

RL: ANT (Analyte); ANST (Analytical study)

(determination of, carbon-labeled androstenedione in, reaction mechanism in relation to)

IT 10028-17-8, Tritium, properties 14762-75-5, Carbon 14, properties

RL: PRP (Properties)

(isotope effect of, in aromatization of androstenedione by aromatase of human placenta)

IT 118790-73-1P, Androst-4-ene-3,17-dione-19-14C

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and aromatase of human placenta determination using, reaction mechanism

in relation to)

IT 118790-74-2P, Androst-4-ene-3,17-dione-19-13C

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and aromatization of, by aromatase of human placenta, reaction mechanism in relation to)

IT 106722-72-9 118790-75-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(substitution reaction of, with epoxyestrane ethylene ketal)

IT 102490-33-5

RL: RCT (Reactant); RACT (Reactant or reagent)

(substitution reaction of, with labeled carbon methylmagnesium compds.)

IT 102490-33-5

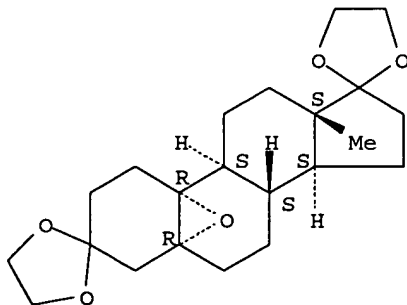
RL: RCT (Reactant); RACT (Reactant or reagent)

(substitution reaction of, with labeled carbon methylmagnesium compds.)

RN 102490-33-5 HCAPLUS

CN Estrane-3,17-dione, 5,10-epoxy-, cyclic bis(1,2-ethanediyl acetal), (5 $\alpha$ ,10 $\alpha$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L25 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN

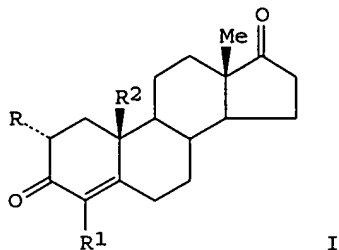
AN 1989:39230 HCAPLUS

DN 110:39230

ED Entered STN: 04 Feb 1989

Search done by Noble Jarrell

TI Interactions of thiol-containing androgens with human placental aromatase  
 AU Bednarski, Patrick J.; Nelson, Sidney D.  
 CS Dep. Med. Chem., Univ. Washington, Seattle, WA, 98195, USA  
 SO Journal of Medicinal Chemistry (1989), 32(1), 203-13  
 CODEN: JMCMAR; ISSN: 0022-2623  
 DT Journal  
 LA English  
 CC 32-4 (Steroids)  
 Section cross-reference(s): 2  
 OS CASREACT 110:39230  
 GI



AB Androgens I (R = R1 = H, R2 = SH, CH<sub>2</sub>C.tplbond.CH; R = SH, R1 = H, R2 = Me; R = H, R1 = OH, R2 = Me) were synthesized and investigated to characterize structural features important for the inhibition of aromatase. Analogs of androstenedione with thiol groups in either the 2 $\alpha$ ,10 $\beta$ -, or 19-positions caused time-dependent inhibition of human placental aromatase. I (R = R1 = H, R2 = SH) proved to be the most potent suicide substrate. However, I (R = R1 = H, R2 = CH<sub>2</sub>SH) was the best all-around inhibitor. All the compds. except I (R = R1 = H, R2 = CH<sub>2</sub>SH) exhibited normal type IP-450 difference spectra with partially purified/solubilized, human placental aromatase. I (R = R1 = H, R2 = CH<sub>2</sub>SH) induced split Soret peaks at 380 and 474 nm, which suggested binding of the 19-thiolate directly to the Fe<sup>3+</sup> of aromatase. This binding could be displaced by aminogluthethimide but not by androstenedione. The inhibitory activity of I (R = R1 = H, R2 = CH<sub>2</sub>SH) may be explained by two independent mechanisms, i.e. suicide inactivation of aromatase in the ferrous state, and a direct hyper-type II binding to the remaining portion of the cytochrome in the ferric state. A free thiol group was necessary for the suicide inhibitory activity of I (R = R1 = H, R2 = CH<sub>2</sub>SH). Aromatase previously inactivated by I could be reactivated after incubation with the disulfide reducing agent dithiothreitol, which suggests that a disulfide bond may be involved in aromatase inactivation by these inhibitors.

ST mercaptoandrosterone prepn aromatase inhibitor; androstenone mercapto prepn aromatase inhibitor

IT 90212-02-5  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (acetylation and inhibition by, of human placental aromatase)

IT 3962-66-1, Estr-5(10)-ene-3,17-dione  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (ketalization of)

IT 9039-48-9, Aromatase  
 RL: PROC (Process)  
 (of human placenta, inhibition of, by mercaptoandrostenones)

IT 63-05-8, Androst-4-ene-3,17-dione  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (oxidation of)

IT 2220-74-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and bromination-hydroxylation of)



IT 117626-53-6P 117626-54-7P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and decarboxylation of)

IT 116168-70-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and dehydration of)

IT 116168-68-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and dehydrobromination of)

IT 7430-11-7P 17503-11-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and deoxygenation-hydroxylation of)

IT 117626-56-9P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and desilylation of)

IT 566-48-3P 77016-85-4P 90212-29-6P 116168-66-2P 117626-50-3P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and inhibition by, of human placental aromatase)

IT 116168-69-5P 117626-55-8P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and ketal cleavage of)

IT 13361-64-3P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and reaction of, with cuprous iodide)

IT 117678-49-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and reaction of, with epoxyestrane-1,2-dione)

IT 117626-51-4P 117626-52-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and reaction of, with xanthate)

IT 102490-33-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and thiolysis of)

IT 571-16-4P 571-17-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and tosylation of)

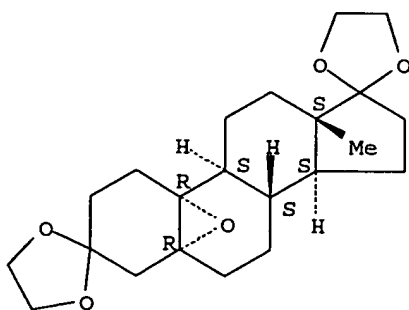
IT 17689-04-2  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (silylation of)

IT 102490-33-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and thiolysis of)

RN 102490-33-5 HCAPLUS

CN Estrane-3,17-dione, 5,10-epoxy-, cyclic bis(1,2-ethanediyl acetal),  
 (5 $\alpha$ ,10 $\alpha$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L25 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1988:510745 HCAPLUS

DN 109:110745

ED Entered STN: 01 Oct 1988

TI Preparation of thiol-substituted steroids as suicide inhibitors of aromatase, useful in the treatment of breast cancer

IN Bednarski, Patrick J.; Porubek, David J.; Nelson, Sidney D.

PA Washington Research Foundation, USA

SO U.S., 14 pp.

CODEN: USXXAM

DT Patent

LA English

IC ICM A61K031-56

ICS C07J001-00

INCL 514170000

CC 32-4 (Steroids)

Section cross-reference(s): 1, 2, 7

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4745109	A	19880517	US 1984-642620	19840820 <--
US 1984-642620		19840820	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 4745109	ICM	A61K031-56
	ICS	C07J001-00
	INCL	514170000
US 4745109	NCL	514/170.000; 514/177.000; 552/523.000; 552/632.000; 552/644.000

OS MARPAT 109:110745

GI For diagram(s), see printed CA Issue.

AB Title steroids I [R1 = thiol (e.g., SH or CH2SH); R2 =  $\beta$ -OH, oxo] were prepared and tested as suicide inhibitors of aromatase. 17 $\beta$ -Estradiol 3-Me ether underwent Birch reduction and subsequent hydrolysis to give 17 $\beta$ -hydroxyestr-5(10)-en-3-one, which was ketalized and acetylated to give 17 $\beta$ -acetoxyster-5(10)-en-3-3-one ethylene ketal. The latter was converted to a bromohydrin, which was cyclized by NaOMe in MeOH to give the 5 $\alpha$ (10 $\alpha$ )-epoxide. Cleavage of the epoxide by NaSH and dehydration of the mercapto alc. gave I (R1 = SH, R2 =  $\beta$ -OH) (II). At 500 nM in a solution containing 1.0 mg human placental microsomal protein/mL and 0.36 mM NADPH, II reduced aromatase activity to 67% of control in 3 min at 30°, whereas 95-96% activity remained when either NADPH or atmospheric O was excluded.

ST thiol steroid prepn aromatase inhibitor; androstenedione mercapto prepn aromatase inhibitor; estrenone mercapto prepn aromatase inhibitor; suicide inhibitor aromatase steroid thiol

IT Estrogens

RL: BPN (Biosynthetic preparation); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(biosynthesis of, inhibitors of, steroidal thiols as)

IT Androgens  
RL: PROC (Process)  
(conversion of, to estrogens, steroidal thiols as inhibitors of)

IT Mammary gland, preparation  
(neoplasm, estrogen-dependent)

IT Neoplasm inhibitors  
(steroidal thiols)

IT Steroids, preparation  
RL: SPN (Synthetic preparation); PREP (Preparation).  
(mercapto, preparation of, from steroidal alc's.)

IT 1035-77-4  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(Birch reduction of)

IT 510-64-5  
RL: PROC (Process)  
(conversion of, to thiol)

IT 1624-62-0  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(ketalization of)

IT 28336-29-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and Birch reduction of)

IT 15342-09-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and acetylation of)

IT 95936-29-1P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and aminolysis of)

IT 2220-74-8P 18367-54-9P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and conversion of, to bromohydrin)

IT 28838-86-0P 116168-68-4P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and cyclization of, epoxide from)

IT 51101-79-2P 116168-70-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and dehydration of)

IT 51101-78-1P 116168-69-5P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and deketalization of)

IT 1238-30-8P 116168-67-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and hydrolysis of)

IT 1089-78-7P 3962-66-1P, Estr-5(10)-ene-3,17-dione  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and ketalization of)

IT 95936-28-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and substitution reaction of, with potassium Et xanthogenate)

IT 24275-29-4P 102490-33-5P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and sulfurization of)

IT 51101-80-5P 90212-02-5P 116168-66-2P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as suicide inhibitor of aromatase)

IT 63-05-8, Androstenedione  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (protection of aromatase from steroidal thiol suicide inhibitors by)

IT 140-89-6, Potassium ethyl xanthogenate  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (substitution reaction of, with triflyloxyandrostenedione)

IT 7782-44-7, Oxygen, uses and miscellaneous  
 RL: USES (Uses)  
 (suicide inhibition of aromatase by steroidal thiols in presence of)

IT 53-57-6, NADPH  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (suicide inhibition of aromatase by steroidal thiols in presence of)

IT 52-90-4, L-Cysteine, uses and miscellaneous  
 RL: USES (Uses)  
 (suicide inhibition of aromatase by steroidal thiols, effect on)

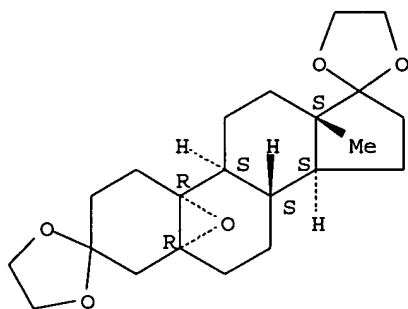
IT 9039-48-9, Aromatase  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (suicide inhibition of, by steroidal thiols)

IT 102490-33-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and sulfurization of)

RN 102490-33-5 HCAPLUS

CN Estrane-3,17-dione, 5,10-epoxy-, cyclic bis(1,2-ethanediyl acetal),  
 (5 $\alpha$ ,10 $\alpha$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L25 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1986:515283 HCAPLUS  
 DN 105:115283  
 ED Entered STN: 03 Oct 1986  
 TI Transition metal phthalocyanines and iodosobenzene as epoxidizing agents  
 IN Rohde, Ralph; Neef, Guenter  
 PA Schering A.-G. , Fed. Rep. Ger.  
 SO Ger. Offen., 13 pp.  
 CODEN: GWXXBX  
 DT Patent  
 LA German  
 IC ICM C07B041-04  
 ICS C07J071-00; C07D301-03; C09B067-12  
 CC 32-3 (Steroids)  
 Section cross-reference(s): 25, 26

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3438484	A1	19860417	DE 1984-3438484	19841017 <--
	DE 3438484	C2	19870619		
PRAI	DE 1984-3438484		19841017	<--	

CLASS

PATENT NO.	CLASS	PATENT	FAMILY CLASSIFICATION CODES
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Search done by Noble Jarrell

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DE 3438484 ICM C07B041-04  
ICS C07J071-00; C07D301-03; C09B067-12

AB Transition metal phthalocyanines and PhIO were used as epoxidizing agents of organic acyclic, cyclic or polycyclic compds. containing  $\geq 1$  C:C double bond, to give an epoxidized compound A solution of 3,3-(2,2-dimethyltrimethylenedioxy)-5(10),9(11)-estradien-17-one in MeCN was treated with PhIO and Fe phthalocyanines and the mixture stirred 3.5 h at room temperature to give 6.7% 3,3-(2,2-dimethyltrimethylenedioxy)-5 $\beta$ ,10 $\beta$ -epoxy-9(11)-estren-17-one and 73.7% the 5 $\alpha$ ,10 $\alpha$ -epoxy isomer.

ST steroid epoxidn phthalocyanine iodosobenzene; double bond epoxidn phthalocyanine iodosobenzene; epoxyestrenone; estrenone epoxy

IT Epoxidation  
(agents for, transition metal phthalocyanines and iodosobenzene as)

IT Steroids, reactions  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(unsatd., epoxidn. of, with transition metal phthalocyanines and iodosobenzene)

IT 55534-06-0 104000-03-5 104000-06-8 104000-08-0 104068-75-9  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(epoxidn. of, with iodosobenzene and iron phthalocyanine)

IT 91175-92-7  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(epoxidn. of, with iodosobenzene and transition metal phthalocyanines)

IT 132-16-1 574-93-6D, transition metal derivs. 3317-67-7 14055-02-8  
14325-24-7  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(iodosobenzene and, epoxidizing agent for unsatd. steroids)

IT 93697-60-0P 104000-04-6P 104000-05-7P 104000-07-9P  
104000-09-1P 104068-76-0P 104068-77-1P 104068-78-2P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, by epoxidn. of unsatd. steroid with iodosobenzene and iron phthalocyanine)

IT 98049-51-5P 104000-02-4P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, with iodosobenzene and transition metal phthalocyanines)

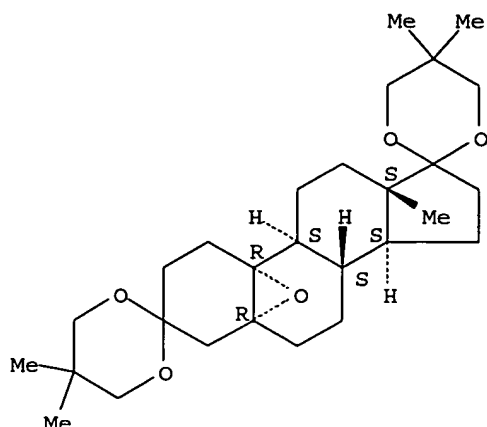
IT 536-80-1  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(transition metal phthalocyanines and, epoxidizing agents for unsatd. steroids)

IT 104000-05-7P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, by epoxidn. of unsatd. steroid with iodosobenzene and iron phthalocyanine)

RN 104000-05-7 HCAPLUS

CN Estrane-3,17-dione, 5,10-epoxy-, cyclic bis(2,2-dimethyl-1,3-propanediyl acetal), (5 $\alpha$ ,10 $\alpha$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L25 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1982:406614 HCAPLUS  
 DN 97:6614  
 ED Entered STN: 12 May 1984  
 TI Selective aromatization of ring B in 19-norsteroids and synthesis of  
 equilenin-type compounds  
 AU Mihailovic, Mihailo L.; Forsek, Joze; Lorenc, Ljubinka  
 CS Dep. Chem., Univ. Belgrade, Belgrade, YU-11001, Yugoslavia  
 SO Journal of the Chemical Society, Perkin Transactions 1: Organic and  
 Bio-Organic Chemistry (1972-1999) (1982), (1), 1-7  
 CODEN: JCPRB4; ISSN: 0300-922X  
 DT Journal  
 LA English  
 CC 32-3 (Steroids)  
 OS CASREACT 97:6614  
 GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Acetoxypoxyestrane I (R2 =  $\beta$ -O, R1R2 = O, R3 = OAc, R4 =  $\alpha$ -H), prepared from I (R2 = bond, R1 = R3 = R4 = H, R2 = OH), by sequential stereoselective epoxidn., oxidation, and stereoselective acetoxylation, underwent selective aromatization of ring B in MeOH/OH- under reflux for 1 h to give estratrienediol II. II underwent sequential diacetylation, bisdeacetalization, and ring A aromatization with Pb(OAc)<sub>4</sub> to give 6,7-diacetoxyequilenin (III).

ST norsteroid selective aromatization; acetoxyequilenin; equilenin acetoxy; epoxysteranone selective aromatization; estranone epoxy selective aromatization

IT 19-Norsteroids  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (7 $\alpha$ -acetoxy-5 $\beta$ ,10 $\beta$ -epoxy-6-oxo, selective aromatization of ring A of)

IT Aromatization  
 (of acetoxypoxyestrane, selective ring B)

IT 17324-86-6  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (epoxidn. of, stereoselective)

IT 1103-94-2P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and acetoxylation of)

IT 69660-94-2P 69660-97-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and acetylation of)

IT 69660-95-3P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and deacetalization of)

IT 81969-02-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and oxidation of)

IT 69660-96-4P 69660-99-7P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and ring A aromatization of)

IT 81901-75-9P 81901-76-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and selective ring B aromatization of)

IT 69660-98-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

IT 2208-12-0P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of, by aromatization of ring A of epoxyestraneol)

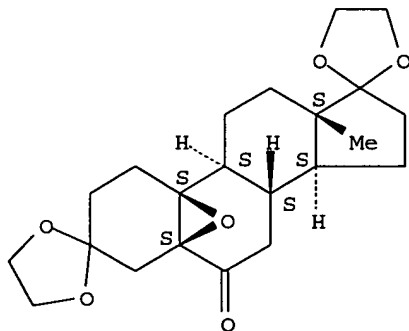
IT 69660-93-1P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation, saponification, and selective ring B aromatization of)

IT 1103-94-2P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and acetoxylation of)

RN 1103-94-2 HCAPLUS

CN Estrane-3,6,17-trione, 5,10-epoxy-, cyclic 3,17-bis(1,2-ethanediyl  
 acetal), (5 $\beta$ )-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

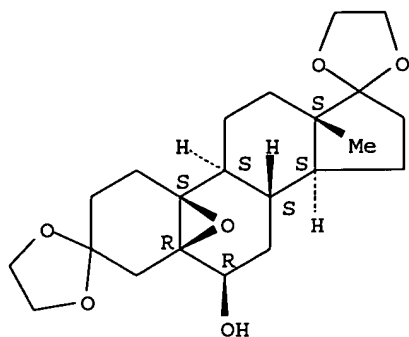


IT 81969-02-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and oxidation of)

RN 81969-02-0 HCAPLUS

CN Estrane-3,17-dione, 5,10-epoxy-6-hydroxy-, cyclic bis(1,2-ethanediyl  
 acetal), (5 $\beta$ ,6 $\beta$ )-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



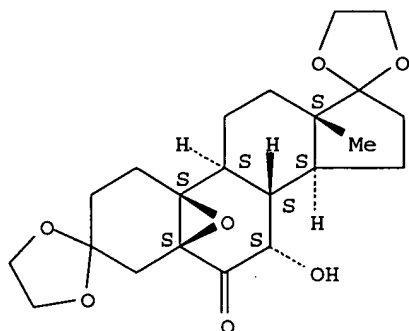
IT 81901-75-9P 81901-76-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and selective ring B aromatization of)

RN 81901-75-9 HCAPLUS

CN Estrane-3,6,17-trione, 5,10-epoxy-7-hydroxy-, cyclic 3,17-bis(1,2-ethanediyl acetal), (5β,7α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 81901-76-0 HCAPLUS

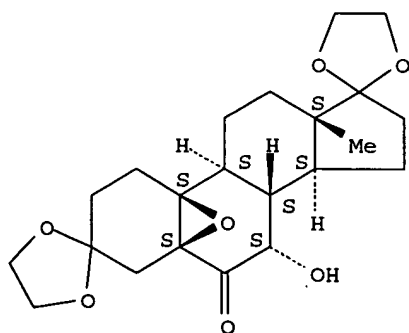
CN Estrane-3,6,17-trione, 5,10-epoxy-7-hydroxy-, cyclic 3,17-bis(1,2-ethanediyl acetal), dimer (9CI) (CA INDEX NAME)

CM 1

CRN 81901-75-9

CMF C22 H30 O7

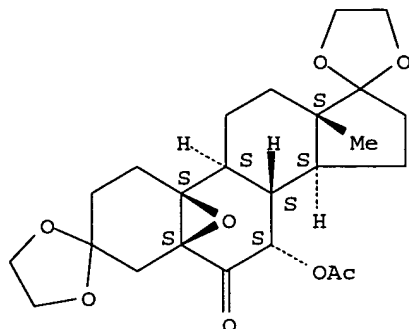
Absolute stereochemistry.



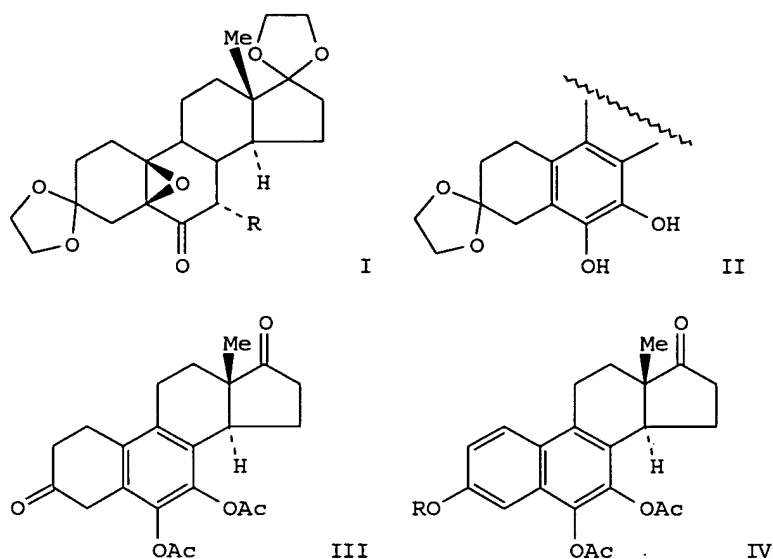


IT 69660-93-1P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation, saponification, and selective ring B aromatization of)  
 RN 69660-93-1 HCAPLUS  
 CN Estrane-3,6,17-trione, 7-(acetyloxy)-5,10-epoxy-, cyclic  
 3,17-bis(1,2-ethanediyl acetal), (5 $\beta$ ,7 $\alpha$ )- (9CI) (CA INDEX  
 NAME)

Absolute stereochemistry.



L25 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1979:152450 HCAPLUS  
 DN 90:152450  
 ED Entered STN: 12 May 1984  
 TI New approach to the aromatization of ring B in 19-norsteroids and to the  
 synthesis of equilenin-type compounds  
 AU Mihailovic, Mihailo Lj.; Forsek, Joze; Lorenc, Ljubinka  
 CS Dep. Chem., Univ. Belgrade, Belgrade, Yugoslavia  
 SO Journal of the Chemical Society, Chemical Communications (1978),  
 (21), 916-18  
 CODEN: JCCCAT; ISSN: 0022-4936  
 DT Journal  
 LA English  
 CC 32-3 (Steroids)  
 GI



AB Heating estranone I (R = OAc), prepared (50-60%) by Pb(OAc)<sub>4</sub> acetoxylation of I (R = H), in alkali gave 80% estratrienediol II with retention of the C-14 configuration. Sequential acetylation (92%) deacetalization (85%), and Pb(OAc)<sub>4</sub> aromatization of the resulting diketone III gave 6,7-diacetoxyequilenin IV (R = H). Acetylation of the latter gave triacetate IV (R = Ac) in 50% overall yield from III.

ST aromatization epoxyestranone equilenin prepn; estranone epoxy aromatization

IT 19-Norsteroids

RL: RCT (Reactant); RACT (Reactant or reagent)

(aromatization of ring B of, equilenin-type compds. by)

IT Aromatization

(of 19-norsteroids, equilenin-type compds. by)

IT 1103-94-2

RL: RCT (Reactant); RACT (Reactant or reagent)

(acetoxylation of)

IT 69660-94-2P 69660-97-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and acetylation of)

IT 69660-93-1P 69660-96-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and aromatization of)

IT 69660-95-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and deacetalization of)

IT 69660-99-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and dehydrogenation of)

IT 69660-98-6P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of, by aromatization of ring B in 19-norsteroids)

IT 1103-94-2

RL: RCT (Reactant); RACT (Reactant or reagent)

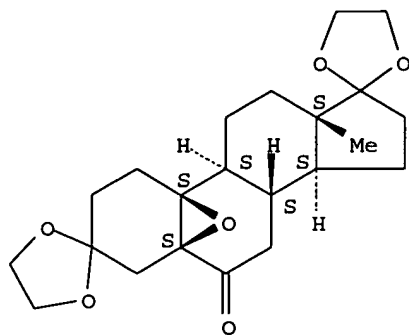
(acetoxylation of)

RN 1103-94-2 HCAPLUS

CN Estrane-3,6,17-trione, 5,10-epoxy-, cyclic 3,17-bis(1,2-ethanediyl)

acetal), (5 $\beta$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



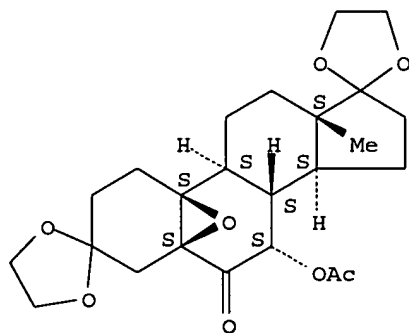
IT 69660-93-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and aromatization of)

RN 69660-93-1 HCAPLUS

CN Estrane-3,6,17-trione, 7-(acetyloxy)-5,10-epoxy-, cyclic 3,17-bis(1,2-ethanediyl acetal), (5 $\beta$ ,7 $\alpha$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L25 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1965:403500 HCAPLUS

DN 63:3500

OREF 63:655g-h,656a-h,657a-b

ED Entered STN: 22 Apr 2001

TI Preparation of phenolic steroids and their ethers

IN Ercoli, Alberto; Gardi, Rinaldo; Pedrali, Cesare

PA Francesco Vesmara, Societa per Azioni

SO 34 pp.

DT Patent

LA Unavailable

CC 42 (Steroids)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	BE 641351		19640616	BE	<--
	DE 1223379			DE	
	FR 1394051			FR	
	NL 302028			NL	
	US 3231567		1966	US	<--

Search done by Noble Jarrell

PRAI IT  
CLASS

19621219 <--

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 3231567	NCL	540/008.000; 204/157.830; 540/010.000; 540/025.000; 540/037.000; 540/076.000; 552/558.000; 552/583.000; 552/606.000; 552/615.000; 552/625.000; 552/630.000; 552/631.000; 552/632.000 <--

AB Treatment of 5,6- and 5,10-disubstituted 3-oxo-19-nor steroids (epoxides, halohydrins, dihalides, dihydroxides) with strong acids leads to ring A aromatic compds. (phenols). In the presence of alcs., phenolic ethers are obtained. A mixture of 3,3:17,17-bis(ethylenedioxy)-19-norandrost-5(6)-ene (I) and norandrost-5(10)-ene (II) (2 g.) (obtained by reduction of 3,3:17,17-bis(ethylenedioxy)-10 $\beta$ -cyano-19-norandrost-5(6)-ene with Na and EtOH) was dissolved in 200 ml. Et<sub>2</sub>O and treated with 20 ml. 15% monoperphthalic acid solution. After standing overnight and washing with 5% NaHCO<sub>3</sub>, saturated NaCl solution, and H<sub>2</sub>O, the solution was dried, evaporated in vacuo, and the residue chromatographed on Florisil to give 1.35 g. 3,3:17,17-bis(ethylenedioxy)-5 $\beta$ ,10 $\beta$ -oxido-19-norandrostane (III), m. 116-17° (MeOH and C<sub>6</sub>H<sub>14</sub>), [ $\alpha$ ]<sub>25D</sub> 10° (CHCl<sub>3</sub>) (eluted with 3:2 C<sub>6</sub>H<sub>6</sub>-Et<sub>2</sub>O), 0.1 g. 3,3:17,17-bis(ethylenedioxy)-5 $\alpha$ ,10 $\alpha$ -oxido-19-norandrostane (IV), m. 120-1°, [ $\alpha$ ]<sub>25D</sub> 20° (CHCl<sub>3</sub>), and 0.37 g. 3,3:17,17-bis(ethylenedioxy)-5 $\alpha$ ,6 $\alpha$ -oxido-19-norandrostane (V), m. 190-1°, [ $\alpha$ ]<sub>25D</sub> -41° (CHCl<sub>3</sub>) (eluted with 1:1 C<sub>6</sub>H<sub>6</sub>-Et<sub>2</sub>O). A solution of 1 g. III in 5 ml. Me<sub>2</sub>CO and 2 drops concentrated HCl was refluxed 2 hrs., concentrated in vacuo, and diluted with H<sub>2</sub>O to give 0.58 g. estrone (VI), m. 253-5°. Similarly, VI was obtained from IV. Reaction of 100 mg. V in 5 ml. AcOH with dry HCl gas during 2 hrs. and dilution with H<sub>2</sub>O gave 46 mg. VI. The crude mixture of III, IV, and V obtained from 2 g. I + II was dissolved in 20 ml. Me<sub>2</sub>CO and 1 ml. concentrated HCl and refluxed 2 hrs. to give VI, m. 258-60°. VI was also prepared by acid treatment of 5 $\beta$ ,10 $\beta$ -oxido-19-norandrostane-3,17-dione (HCl) and 5 $\alpha$ -hydroxy-6 $\beta$ -bromo-19-norandrostane-3,17-dione [(CO<sub>2</sub>H)<sub>2</sub>]. A solution of 100 mg. III in 5 ml. MeOH and 2 drops concentrated HCl was refluxed 1/2 hr., concentrated, diluted with H<sub>2</sub>O, and the precipitate recrystd. from MeOH to give

VI methyl ether (VII), m. 169-70°, [ $\alpha$ ]<sub>25D</sub> 162° (CHCl<sub>3</sub>). VII was also obtained by refluxing 70 mg. 5 $\alpha$ -bromo-10 $\beta$ -hydroxy-19-norandrostane-3,17-dione 1/2 hr. in 5 ml. MeOH (yield 49 mg., m. 168-9° (MeOH)) (no acid added), by refluxing 100 mg. 5 $\alpha$ ,10 $\beta$ -dibromo-19-norandrostane-3,17-dione in 5 ml. C<sub>6</sub>H<sub>6</sub> and 1 ml. MeOH 1/2 hr. (yield 55 mg.) (no acid added), by refluxing 100 mg. 5 $\alpha$ ,6 $\beta$ -dihydroxy-19-norandrostane-3,17-dione in 5 ml. MeOH and 2 drops concentrated HCl 1/2 hr. (yield 46 mg.), and similarly from 100 mg. 5 $\alpha$ -hydroxy-6 $\beta$ -fluoro-19-norandrostane-3,17-dione (yield 100%). A solution of 100 mg. III in 5 ml. cyclopentanol and 2 drops concentrated HCl was refluxed 1 hr. and evaporated in vacuo. The residue was crystallized from MeOH to give 42 mg. VI cyclopentyl ether (VIII), m. 152-3° (MeOH), [ $\alpha$ ]<sub>25D</sub> 136° (dioxane). Similarly, 100 mg. 5 $\alpha$ ,10 $\beta$ -dihydroxy-19-norandrostane-3,17-dione gave 64 mg. VIII, and 100 mg. 5 $\alpha$ -hydroxy-10 $\beta$ -bromo-19-norandrostane-3,17-dione, heated 1 hr. with 5 ml. cyclopentanol and 0.5 ml. HCO<sub>2</sub>H, yielded 42 mg. VIII. When 200 mg. V was refluxed 2 hrs. in 10 ml. cyclohexanol and concentrated HCl, VI cyclohexyl ether, m. 156-7°, [ $\alpha$ ]<sub>25D</sub> 134° (dioxane), was obtained, while III in PhCH<sub>2</sub>OH gave 80% VI benzyl ether, m. 129-30°, [ $\alpha$ ]<sub>25D</sub> 132° (dioxane). A solution of 1 g. V in 20 ml. Me<sub>2</sub>CO, 0.5 g. cetyl alc., and 2 drops concentrated HCl was refluxed 2 hrs. to give VI cetyl ether (IX), m. 67-8°, [ $\alpha$ ]<sub>25D</sub> 95° (dioxane). Similarly prepared were VI nonyl ether, m. 56-8°, [ $\alpha$ ]<sub>25D</sub> 114° (dioxane) and VI ethyl ether, m. 126°, [ $\alpha$ ]<sub>25D</sub> 150° (dioxane). IX was also obtained from 5 $\alpha$ -bromo-6 $\beta$ -hydroxy-19-norandrostane-3,17-dione. Similarly, 1 g. 5 $\alpha$ ,6 $\beta$ -dibromo-19-norandrostane-3,17-dione in 20 ml. Me<sub>2</sub>CO, 0.5 g. cinnamyl alc., and 0.2 ml. concentrated HCl gave VI cinnamyl ether, m. 144-5°. Also prepared was VI allyl ether, m.

107-8°,  $[\alpha]_{25D} 144^\circ$  (dioxane). A solution of 5 $\beta$ ,10 $\beta$ -oxido-17 $\beta$ -hydroxy-19-norandrostane-3-one in 5 ml. Me<sub>2</sub>CO and 2 drops concentrated HCl was refluxed 1/2 hr. and diluted with H<sub>2</sub>O to give estradiol which was also prepared from 6 $\beta$ -fluoro-5 $\alpha$ ,17 $\beta$ -dihydroxy-19-norandrostane-3-one. A solution of 2 g. 3,3-ethylenedioxy-17 $\alpha$ -ethynyl-17 $\beta$ -hydroxy-19-norandrost-5-ene in 150 ml. Et<sub>2</sub>O was treated with 10 ml. 20% PhCO<sub>3</sub>H solution. After standing overnight, washing with 5% NaHCO<sub>3</sub>, saturated NaCl solution, and H<sub>2</sub>O, and evaporation, the residue was dissolved in 20 ml. cyclopentanol and 1 ml. concentrated HCl, and the solution refluxed 2 hrs. and diluted with H<sub>2</sub>O to give 17 $\alpha$ -ethynylestradiol 3-cyclopentyl ether (X), m. 107-8°,  $[\alpha]_{25D} 5^\circ$  (dioxane). Similarly prepared were the cyclopentyl ethers of 17 $\alpha$ -methylestradiol, m. 107-8°,  $[\alpha]_{22D} 45^\circ$  (dioxane), and of 17 $\alpha$ -ethylestradiol, m. 122-4°,  $[\alpha]_{22D} 43.5^\circ$  (dioxane). X was also obtained from 10 $\beta$ -fluoro-5 $\alpha$ , 17 $\beta$ -dihydroxy-17 $\alpha$ -ethynyl-19-norandrostane-3-one. When 2 g. 3,3-ethylenedioxy-5 $\beta$ ,10 $\beta$ -oxido-17 $\alpha$ -ethynyl-17 $\beta$ -hydroxy-19-norandrostane were refluxed 1/2 hr. in 20 ml. MeOH with 30 mg. MeC<sub>6</sub>H<sub>4</sub>SO<sub>3</sub>H, 17 $\alpha$ -ethynylestradiol 3-methyl ether (XI) was obtained. Similarly, 100 mg. 3,3-ethylenedioxy-5 $\alpha$ -fluoro-10 $\beta$ ,17 $\beta$ -dihydroxy-17 $\alpha$ -ethynyl-19-norandrostane in MeOH and HCl (1/2 hr. reflux) gave 76 mg. XI, m. 150-1°,  $[\alpha]_{25D} 2.3^\circ$  (dioxane). A solution of 2 g. of a mixture of 3,3:20,20-bis(ethylenedioxy)-19-norpregn-5(6)-ene and norpregn-5(10)-ene (obtained by reduction of 3,3:20,20-bis(ethylenedioxy)-10 $\beta$ -cyano-19-norpregn-5(6)-ene with Na and EtOH) in 200 ml. Et<sub>2</sub>O was treated with 60 ml. 15% monoperphthalic acid as described for III, IV, and V. The crude reaction product (.apprx.2 g.) was dissolved in 15 ml. Me<sub>2</sub>CO and 0.5 ml. H<sub>2</sub>SO<sub>4</sub> and refluxed 2 hrs. Evaporation in vacuo and dilution with H<sub>2</sub>O gave 0.6 g. 3-hydroxy-17-acetylestria-1,3,5(10)-triene (XII), m. 247-9°,  $[\alpha]_{25D} 159^\circ$  (CHCl<sub>3</sub>). The epoxides prepared in the preceding experiment were separated by chromatography on Florisil to give (elution with 3:2 C<sub>6</sub>H<sub>6</sub>:Et<sub>2</sub>O) 3,3:20,20-bis(ethylenedioxy)-5 $\beta$ ,10 $\beta$ -oxido-19-norpregnane (XIII), m. 136-7°,  $[\alpha]_{25D} 58^\circ$  (CHCl<sub>3</sub>), and 3,3:20,20-bis(ethylenedioxy)-5 $\alpha$ ,6 $\alpha$ -oxido-19-norpregnane (XIV) (not characterized). Refluxing 1 g. XIII 2 hrs. in 5 ml. Me<sub>2</sub>CO and 2 drops H<sub>2</sub>SO<sub>4</sub>, concentration in vacuo, and dilution with H<sub>2</sub>O gave 0.6 g. XII. Similarly, 1 g. XIV in 50 ml. AcOH treated 2 hrs. with HCl gas and dilution with H<sub>2</sub>O gave 450 mg. XII. A solution of 1 g. 10 $\beta$ -fluoro-5 $\alpha$ -hydroxy-19-norpregnane-3,20-dione in 5 ml. Me<sub>2</sub>CO was refluxed 2 hrs. with 20 mg. sulfosalicylic acid and gave 0.6 g. XII. When 0.5 g. XIII was dissolved in 25 ml. MeOH and 2 drops concentrated HCl, the solution kept 1 hr. at room temperature and diluted with H<sub>2</sub>O, and the precipitate recrystd. from MeOH, XII methyl ether, m. 134-6°,  $[\alpha]_{25D} 160^\circ$  (CHCl<sub>3</sub>), was obtained. Reaction of 5 $\alpha$ -chloro-10 $\beta$ -hydroxy-19-norpregnane-3,20-dione with cyclopentanol and concentrated HCl (ratio 20:1) (2 hrs. reflux) gave XII cyclopentyl ether, m. 116-17°,  $[\alpha]_{25D} 138^\circ$  (dioxane). The crude epoxides obtained from 850 mg. 3,3-ethylenedioxy-17 $\alpha$ -acetoxy-19-norpregn-5-en-20-one in 80 ml. Et<sub>2</sub>O and 5 ml. 15% monoperphthalic acid in Et<sub>2</sub>O were dissolved in 15 ml. Me<sub>2</sub>CO and 0.5 ml. concentrated HCl and refluxed 2 hrs. to give, after evaporation and dilution with H<sub>2</sub>O, 3-hydroxy-17 $\alpha$ -acetoxy-17 $\beta$ -acetylestria-1,3,5(10)-triene, m. 242-4°,  $[\alpha]_{25D} 49^\circ$  (CHCl<sub>3</sub>). A solution of 1 g. 3,3:20,20-bis(ethylenedioxy)-17 $\alpha$ -hydroxy-19-norpregn-5-ene in 50 ml. Et<sub>2</sub>O was treated with 15 ml. PhCO<sub>3</sub>H solution. The crude mixture of epoxides was refluxed 2 hrs. in 15 ml. Me<sub>2</sub>CO and 0.5 ml. H<sub>2</sub>SO<sub>4</sub> to give 3,17 $\alpha$ -dihydroxy-17 $\beta$ -acetylestria-1,3,5(10)-triene (XV), m. 240-2°,  $[\alpha]_{25D} 90.5^\circ$  (dioxane). From the mixture of epoxides, the 5 $\beta$ ,10 $\beta$ -oxido compound was separated by recrystn. from MeOH, and 1 g. was refluxed 1/2 hr. in 50 ml. MeOH with 100 mg. MeC<sub>6</sub>H<sub>4</sub>SO<sub>3</sub>H to give XV methyl ether, m. 150-2° (MeOH),  $[\alpha]_{25D} 45.5^\circ$  (dioxane). Ir spectra are reported for III, IV, and V.

## IT Steroids

(3-hydroxy  $\Delta^{1,3,5(10)}$ -, and ethers thereof)

## IT Spectra, infrared

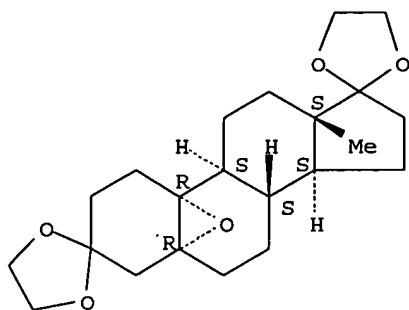
(of 5,10-epoxy-5 $\alpha$ -estrane-3,17-dione cyclic bis(ethylene acetal))

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IT 5 $\alpha$ -Estrae-3,17-dione, 5,6 $\alpha$ -epoxy-, cyclic bis(ethylene acetal)
IT 72-33-3, 19-Nor-17 $\alpha$ -pregna-1,3,5(10)-trien-20-yn-17-ol, 3-methoxy-
152-43-2, 19-Nor-17 $\alpha$ -pregna-1,3,5(10)-trien-20-yn-17-ol,
3-(cyclopentyloxy)- 858-98-0, Estra-1,3,5(10-trien-17-one,
3-(benzyloxy)- 1474-50-6, Estra-1,3,5(10-trien-17-one, 3-ethoxy-
1624-56-2, 19-Norpregna-1,3,5(10)-trien-20-one, 3-(cyclopentyloxy)-
1624-57-3, 19-Norpregna-1,3,5(10)-trien-20-one, 3,17-dihydroxy-
1624-58-4, 19-Norpregna-1,3,5(10)-trien-20-one, 17-hydroxy-3-methoxy-
1624-60-8, 5 $\beta$ -Estrane-3,17-dione, 5,10-epoxy-, cyclic
bis(ethylene acetal) 1624-62-0, Estra-1,3,5(10-trien-17-one, 3-methoxy-
1624-63-1, Estra-1,3,5(10-trien-17-one, 3-(cyclohexyloxy)- 1624-64-2,
Estra-1,3,5(10-trien-17-one, 3-(nonyloxy)- 1624-66-4,
Estra-1,3,5(10-trien-17-one, 3-(cinnamyloxy)- 1624-67-5,
Estra-1,3,5(10-trien-17-one, 3-(allyloxy)- 1624-69-7,
Estra-1,3,5(10)-trien-17 $\beta$ -ol, 3-(cyclopentyloxy)-17-methyl-
1624-70-0, 19-Nor-17 $\alpha$ -pregna-1,3,5(10)-trien-17-ol,
3-(cyclopentyloxy)- 1624-72-2, 19-Nor-5 $\beta$ -pregnane-3,20-dione,
5,10-epoxy-, cyclic bis(ethylene acetal) 1624-73-3, 19-Norpregna-
1,3,5(10)-trien-20-one, 3-methoxy- 1624-74-4, 19-Norpregna-1,3,5(10)-
trien-20-one, 3,17-dihydroxy-, 17-acetate 1624-75-5,
Pregn-4-ene-3,20-dione, 6 $\alpha$ -amino- 1667-98-7, 19-Norpregna-
1,3,5(10)-trien-20-one, 3-hydroxy- 1805-17-0, Estra-1,3,5(10-trien-17-
one, 3-(hexadecyloxy)- 1852-81-9, Estra-1,3,5(10-trien-17-one,
3-(cyclopentyloxy)- 2027-44-3, Pregn-4-ene-3,20-dione,
6 $\beta$ -acetamido- 2454-33-3, Pregn-4-ene-3,20-dione,
6 $\alpha$ -acetamido- 102490-33-5, 5 $\alpha$ ,10 $\alpha$ -Estrane-3,17-
dione, 5,10-epoxy-, cyclic bis(ethylene acetal)
(preparation of)
IT 166-68-7, Dispiro[1,3-dioxolane-2,3'(4'H)-[5,10]epoxy[17H]cyclopenta[a]phe-
nanthrene-17',2''-[1,3]dioxolane] 175-26-8, Dispiro[1,3-dioxolane-
2,3'(4'H)-[5,6]epoxy[5H]cyclopenta[a]phenanthrene-17'(2'H),2''-
[1,3]dioxolane]
(steroid derivs.)
IT 1624-60-8, 5 $\beta$ -Estrane-3,17-dione, 5,10-epoxy-, cyclic
bis(ethylene acetal) 102490-33-5, 5 $\alpha$ ,10 $\alpha$ -Estrane-
3,17-dione, 5,10-epoxy-, cyclic bis(ethylene acetal)
(preparation of)
RN 1624-60-8 HCAPLUS
CN Estrane-3,17-dione, 5,10-epoxy-, cyclic bis(1,2-ethanediyl acetal),
(5 $\beta$ )-(9CI) (CA INDEX NAME)

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Absolute stereochemistry.



L25 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1965:403499 HCAPLUS

DN 63:3499

OREF 63:655e-g

ED Entered STN: 22 Apr 2001

TI 20-Oxo-16-pregnene derivatives

IN Magyar, Gyorgy; Bite, Pal

PA Gedeon Richter Vegyeszeti Gyar R. T.

SO 3 pp.

DT Patent

LA Unavailable

CC 42 (Steroids)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	AT 239970		19650510	AT	<--
PRAI	HU		19600323	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
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AB In a process for preparing 20-oxo-16-pregnene derivs. from steroid sapogenins or from solanum alkaloids the starting compound is acylated, isomerized, oxidized, and the  $\delta$ -acyloxy- or  $\delta$ -acylaminoisocaprofonate group is removed by treatment with a mineral acid at elevated temperature in the presence of a H<sub>2</sub>O-immiscible organic solvent, e.g. benzene, toluene, xylene, dichloroethylene, the mineral acid being used in an amount of  $\leq 5\%$  by weight of the reaction product. Preferably, benzene is used as solvent, and the cleavage is effected at the b.p. of the reaction mixture and with 1-3% concentrated HCl. Thus, using solasodine as starting material, 5,16-pregnadien-3 $\beta$ -ol-20-one acetate, m. 170-2°, and 5,16-pregnadienolone propionate, m. 172-4°, were obtained. From tomatidine, 5 $\alpha$ -pregn-16-en-3 $\beta$ -ol-20-one acetate, m. 163-4°, and the resp. propionate, m. 182-4°, were obtained. Diosgenine was also used as starting material to obtain the acetate and propionate of 15,16-pregnadienolone. The compds. are useful as intermediates in the manufacture of steroid hormones.

IT Steroids

(20-keto  $\Delta$ 16-, from sapogenins and solanum alkaloids)

IT Solanum

(alkaloids, pregn-16-en-20-one derivative preparation from)

IT Sapogenins

(pregn-16-en-20-one derivs. from)

IT 979-02-2, Pregna-5,16-dien-20-one, 3 $\beta$ -hydroxy-, acetate 1169-20-6,

5 $\alpha$ -Pregn-16-en-20-one, 3 $\beta$ -hydroxy-, acetate 1624-98-2,

5 $\alpha$ -Pregn-16-en-20-one, 3 $\beta$ -hydroxy-, propionate 3285-87-8,

Pregna-5,16-dien-20-one, 3 $\beta$ -hydroxy-, propionate

(preparation of)

L25 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1965:3268 HCAPLUS

DN 62:3268  
 OREF 62:621c-h,622a  
 ED Entered STN: 22 Apr 2001  
 TI Preparation of 19-norsteroids, particularly  $\Delta^5(10)$ -19-norsteroids  
 oxygenated in 6-position  
 PA CIBA Ltd.  
 SO 20 pp.  
 DT Patent  
 LA Unavailable  
 IC C07C  
 CC 42 (Steroids)  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 1369017		19640807	FR	<--
	GB 1011573			GB	
	NL 295431			NL	
	US 3178419		1965	US	<--
PRAI CH			19620718	<--	

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
FR 1369017	IC	C07C
US 3178419	NCL	540/008.000; 540/017.000; 540/023.000; 540/025.000; 540/076.000; 540/105.000; 552/561.000; 552/583.000; 552/586.000; 552/590.000; 552/606.000; 552/607.000; 552/615.000; 552/633.000; 552/636.000; 552/637.000; 552/638.000; 552/639.000; 552/646.000; 552/650.000 <--

OS CASREACT 62:3268

AB The title compds. are prepared from  $\Delta^5$ -19-hydroxysteroids by oxidation with  $\text{Pb}(\text{OAc})_4$ . Acetylation of 8.6 g. 19-hydroxyandrost-4-ene-3,17-dione in 50 ml.  $\text{Ac}_2\text{O}$  and 50 ml.  $\text{C}_5\text{H}_5\text{N}$  gave an oily acetate which was refluxed 22 hrs. with 500 ml.  $\text{C}_6\text{H}_6$ , 50 ml.  $(\text{CH}_2\text{OH})_2$ , and 500 mg.  $\text{TsOH}$  ( $\text{Ts}$  = tosyl). The mixture was poured on ice and extracted with  $\text{Et}_2\text{O}$ , the extract washed with  $\text{NaHCO}_3$  and evaporated, and the oily residue refluxed 1 hr. with 400 ml. 5% methanolic  $\text{KOH}$ . Dropwise addition of  $\text{H}_2\text{O}$  gave a precipitate, which was taken up in  $\text{AcOEt}$  and filtered off on  $\text{Al}_2\text{O}_3$ , then recrystd. from  $\text{Me}_2\text{CO}$ -petr. ether to give 6.8 g. 3,3:17,17-bis(ethylenedioxy)-19-hydroxyandrost-5-ene (I), m. 199-200°,  $[\alpha]_D^{25}$  -59°. A mixture of 3.25 g. dry  $\text{Pb}(\text{OAc})_4$  and 3.25 g.  $\text{CaCO}_3$  was refluxed briefly in 175 ml. absolute  $\text{C}_6\text{H}_6$ , cooled, refluxed 6 hrs. after addition of 3.25 g. I, and kept overnight at room temperature. The resulting oil (3.5 g.), after chromatography on silica gel was saponified with 250 ml. 5% methanolic  $\text{KOH}$  (1 hr. room temperature) and gave 2.71 g. 3,3:17,17-bis(ethylenedioxy)-6-hydroxy-19-norandrost-5(10)-ene (II), m. 150-2° ( $\text{Me}_2\text{CO}$ -petr. ether); after 3 more recrystns. m. 157-8°,  $[\alpha]_D^{25}$  73°. Similarly prepared was 1 g. 3,3:20,20-bis(ethylenedioxy)-6-hydroxy-19-norpregn-5(10)ene from 1.5 g. 3,3:20,20-bis(ethylenedioxy)-19-hydroxypregn-5-ene. A solution of 2.715 g. II in 46 ml.  $\text{CHCl}_3$  containing 2.37 g.  $\text{BzOOH}$  was kept overnight at 4°, diluted with  $\text{Et}_2\text{O}$ , and poured on ice. The organic phase was washed with  $\text{KI}$ ,  $\text{Na}_2\text{S}_2\text{O}_3$ ,  $\text{H}_2\text{O}$ ,  $\text{NaHCO}_3$ , and  $\text{H}_2\text{O}$  and the crude product chromatographed to yield 3,3:17,17-bis(ethylenedioxy)-5,10-oxido-6-hydroxy-19-norandrostane (III) 1.336 g., m. 133° ( $\text{Me}_2\text{CO}$ -petr. ether),  $[\alpha]_D^{25}$  12°. A solution of 245 mg. III in little  $\text{C}_5\text{H}_5\text{N}$  was added dropwise to 250 mg.  $\text{CrO}_3$  in 1 ml.  $\text{C}_5\text{H}_5\text{N}$  and the mixture kept overnight to give 227 mg. 3,3:17,17-bis(ethylenedioxy)-5,10-oxido-19-norandrost-6-one (IV), m. 137-8° (2 +  $\text{Me}_2\text{CO}$ -petr. ether),  $[\alpha]_D^{25}$  -94°. A mixture of 200 mg. II and 500 mg. (iso-Pr) $_3\text{Al}$  in 40 ml. absolute  $\text{C}_6\text{H}_6$  and 4 ml.  $\text{Me}_2\text{CO}$  refluxed 16 hrs. yielded 197 mg. crude product which was dissolved in 9:1  $\text{C}_6\text{H}_6$ - $\text{Et}_2\text{O}$  and filtered through  $\text{Al}_2\text{O}_3$  to give 160 mg. 3,3:17,17-bis(ethylenedioxy)-19-norandrost-5(10)-en-6-one (V), m. 178-80° (2 +  $\text{Me}_2\text{CO}$ -petr. ether),  $[\alpha]_D^{25}$  43°. A solution of 470 mg. V in 15 ml.  $\text{AcOH}$ , 15 ml.  $\text{MeOH}$ , and 7 drops  $\text{H}_2\text{O}$  was heated 1 hr. at 60°. The crude reaction product (490 mg.) was filtered in 1:1  $\text{C}_6\text{H}_6$ - $\text{Et}_2\text{O}$  through  $\text{Al}_2\text{O}_3$  to give 406 mg. 3,3-ethylenedioxy-19-norandrost-5(10)-ene-6,17-dione (VI), m. 189-90° (3 +  $\text{Me}_2\text{CO}$ -petr. ether),  $[\alpha]_D^{25}$  167°. VI



(250 mg.) in 10 ml. AcOH was refluxed 1 hr. and evaporated in vacuo. Chromatography of the residue on Al<sub>2</sub>O<sub>3</sub> gave 136 mg. 19-norandrost-5(10)-ene-3,6,17-trione (VII), m. 163° (3 + Me<sub>2</sub>CO-petr. ether). A solution of 1 g. V in 10 ml. EtOH, 31 ml. diethylene glycol, and 10 ml. N<sub>2</sub>H<sub>4</sub>.H<sub>2</sub>O was refluxed 1.5 hrs., cooled, and heated again 30 min. at 100° after addition of 5 g. KOH, 60 ml. diethylene glycol was added, EtOH distilled, and the temperature raised to 190°. The mixture was refluxed 3.25 hrs. and the reaction product isolated, and chromatographed on Al<sub>2</sub>O<sub>3</sub> to give 483 mg. 3,3:17,17-bis(ethylenedioxy)19-norandrost-5-ene (VIII), m. 135-7° (2 + Me<sub>2</sub>CO-petr. ether), [α]<sub>D</sub> -- 196°. VIII (40 mg.) was refluxed 1 hr. with 6 ml. AcOH and 10 drops H<sub>2</sub>O, the solution evaporated in vacuo, and the residue in Et<sub>2</sub>O filtered through Al<sub>2</sub>O<sub>3</sub> to give 20 mg. product, m. 163-4° (twice, Me<sub>2</sub>CO-petr. ether) and proved to be identical with 19-norandrost-4-ene-3,17-dione. To a solution of 3 g. Pb(OAc)<sub>4</sub> and 2 g. BaCO<sub>3</sub> in 150 ml. cyclohexane, heated briefly to boil, was added 2 g. 3β,17β-diacetoxy-19-hydroxyandrost-5-ene, m. 148-9°. The mixture was refluxed 8 hrs. and evaporated in vacuo after removal of the inorg. salts. The residue was dissolved in 100 ml. 3:1 MeOH-H<sub>2</sub>O and the solution refluxed 2 hrs. with 2 g. K<sub>2</sub>CO<sub>3</sub> to give 1.4 g. crude 3β,6,17β-trihydroxy-19-norandrost-5(10)-ene, which was dissolved in 50 ml. Me<sub>2</sub>CO and oxidized with 2 ml. 8N CrO<sub>3</sub>-solution in H<sub>2</sub>SO<sub>4</sub> (1 hr., 0°). Crystallization from Me<sub>2</sub>CO-petr. ether yielded 980 mg. VII, m. 163°, [α]<sub>D</sub> 219°. Similarly, 3β,20β-diacetoxy-19-hydroxy-pregn-5-ene was converted in 50% yield to 19-norpregn-5(10)-ene-3,6,20-trione. Ir and uv data are given.

## IT Norsteroids

(19-, 6-oxy Δ<sup>5</sup>(10)-)

## IT Spectra, visible and ultraviolet

(of 5,10-epoxyestrane-3,6,17-trione cyclic 3,17-bis(ethylene acetal) and congeners)

## IT 5β-Estrane-3,17-dione, 5,10-epoxy-6-hydroxy-, cyclic bis(ethylene acetal)

5β-Estrane-3,6,17-trione, 5,10-epoxy-, cyclic 3,17-bis(ethylene acetal)

## IT 1091-89-0, Estr-5(10)-ene-3,6,17-trione 1240-11-5, Estr-5(10)-ene-3,6,17-trione, cyclic 3-(ethylene acetal) 1243-85-2, Estr-5-ene-3,17-dione, cyclic bis(ethylene acetal) 1246-95-3, Estr-5(10)-ene-3,17-dione, 6-hydroxy-, cyclic bis(ethylene acetal) 1246-96-4, Estr-5(10)-ene-3,6,17-trione, cyclic 3,17-bis(ethylene acetal) 1249-35-0, Androst-5-ene-3,17-dione, 19-hydroxy-, cyclic bis(ethylene acetal) 1249-36-1, Androst-5-ene-3β,17β,19-triol, 3,17-diacetate 1253-50-5, Pregn-5-ene-3,20-dione, 19-hydroxy-, cyclic bis(ethylene acetal) (preparation of)

IT 546-67-8, Lead acetate, Pb(OAc)<sub>4</sub>

(reactions of, with 19-hydroxyandrost-5-ene-3,17-dione cyclic bis(ethylene acetal))

## IT 166-68-7, Dispiro[1,3-dioxolane-2,3' (4'H) - [5,10]epoxy[17H]cyclopenta[a]phenanthrene-17',2'' - [1,3]dioxolane] 187-08-6, Dispiro[1,3-dioxolane-2,3' - [3H]cyclopenta[a]phenanthrene-17' (2'H),2'' - [1,3]dioxolane] (steroid derivs.)

L25 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1965:3267 HCAPLUS

DN 62:3267

OREF 62:620g-h,621a-c

ED Entered STN: 22 Apr 2001

TI 11β,12β-Epoxy pregnane-3,20-dione

IN Julian, Percy L.; Magnani, Arthur

PA Smith Kline &amp; French Laboratories

SO 8 pp.

DT Patent

LA Unavailable

INCL 260239550

CC 42 (Steroids)

FAN.CNT 1

PATENT NO.

KIND

DATE

APPLICATION NO.

DATE

Search done by Noble Jarrell

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 PI US 3153646 19641020 US 19570321 <--

## CLASS

PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES  
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US 3153646 INCL 260239550  
 US 3153646 NCL 540/082.000; 552/535.000; 552/584.000; 552/587.000;  
 552/588.000 <--

GI For diagram(s), see printed CA Issue.

AB In addition to the information in Brit. 846,045 (CA 55, 10508g) the following new procedures were described. 11 $\beta$ ,12 $\beta$ -Epoxy pregnane-3 $\beta$ ,20 $\beta$ -diol (I) (2 g.) in 20 cc. C<sub>5</sub>H<sub>5</sub>N added to 3 g. CrO<sub>3</sub> suspended in 30 cc. C<sub>5</sub>H<sub>5</sub>N and the mixture left 16 hrs. gave 1.35 g. 11 $\beta$ ,12 $\beta$ -epoxy pregnane-3,20-dione (II), m. 142-4° (Me<sub>2</sub>CO). II (34.3 g.) in 450 cc. Me<sub>2</sub>CO treated under cooling with 80 cc. 4N HBr gave 40.5 g. 12 $\alpha$ -bromopregnan-11 $\beta$ -ol-3,20-dione (III), m. 239-40°. Br (11 g.) in 100 cc. HCONMe<sub>2</sub> stirred and heated 15 min. at 45° with 25.6 g. III in 250 cc. HCONMe<sub>2</sub> and 400 mg. p-MeC<sub>6</sub>H<sub>4</sub>SO<sub>3</sub>H gave 28 g. 4,12-dibromopregnan-11 $\beta$ -ol-3,20-dione (IV), m. 218-20° (Me<sub>2</sub>CO). IV (21.8 g.), 175 cc. HCONMe<sub>2</sub>, and 5.7 g. LiCl heated 3 hrs. at 94-6° under N gave 14.5 g. 12 $\alpha$ -bromopregn-4-ene-11 $\beta$ -ol-3,20-dione (V), m. 218-20°. V (2.97 g.), 30 cc. MeOH, 6 cc. H<sub>2</sub>O, and 1.5 g. K<sub>2</sub>CO<sub>3</sub> refluxed 15 min. gave 11 $\beta$ ,12 $\beta$ -epoxy pregn-4-ene-3,20-dione, m. 168-70° (Me<sub>2</sub>CO). Pregn-11-ene-3,20-dione (2 g.) in 50 cc. Et<sub>2</sub>O left 24 hrs. at 25° with 10% excess monoperphthalic acid in Et<sub>2</sub>O gave 11 $\alpha$ ,12 $\alpha$ -epoxy pregnane-3,20-dione. The allo isomer of I (5 g.), 5 cc. C<sub>5</sub>H<sub>5</sub>N, 40 cc. AcOH, and 5 cc. H<sub>2</sub>O treated in the cold with 4 g. CrO<sub>3</sub> in aqueous AcOH, and the mixture left 5 hrs. at room temperature and worked up gave 11 $\beta$ ,12 $\beta$ -epoxyallo pregnane-3,20-dione. 11 $\beta$ ,12 $\beta$ -Epoxy pregnan-21-ol-3,20-dione acetate (VI) left overnight with NaOMe-MeOH gave 11 $\beta$ ,12 $\beta$ -epoxy pregnan-21-ol-3,20-dione (VII). 11 $\beta$ ,12 $\beta$ -Epoxy pregnan-21-ol-3,20-dione 21-propionate was obtained by treatment of the 11,12-dibromo compound with Na propionate and NaHCO<sub>3</sub>, followed by oxidation with CrO<sub>3</sub> in C<sub>5</sub>H<sub>5</sub>N. VII (1 g.) in 25 cc. Me<sub>2</sub>CO and 0.5 ml. C<sub>5</sub>H<sub>5</sub>N left overnight at room temperature with 0.5 g. succinic anhydride gave the hemisuccinate, which treated with Na and Et<sub>2</sub>O gave the Na salt. VI (5 g.) in dioxane left several hrs. at room temperature with 10 cc. HBr-dioxane gave 12-bromopregnane-11 $\beta$ ,21-diol-3,20-dione 21-acetate (VIII). VIII (5.3 g.) in HCONMe<sub>2</sub> and a trace of p-MeC<sub>6</sub>H<sub>4</sub>SO<sub>3</sub>H with 2.2 g. Br gave 4,12-dibromopregnane-11 $\beta$ ,21-diol-3,20-dione 21-acetate (IX). IX (5 g.) in 50 cc. C<sub>5</sub>H<sub>5</sub>N was heated to effect dehydrobromination, and 1.5 g. of the product refluxed several hrs. with 25 cc. Me<sub>2</sub>CO, 3.7 g. KOAc, and 330 mg. NaHCO<sub>3</sub> to give 11 $\beta$ ,12 $\beta$ -epoxy pregn-4-en-21-ol-3,20-dione 21-acetate (X). X (750 mg.) treated with dilute NaOH gave 11 $\beta$ ,12 $\beta$ -epoxy pregn-4-en-21-ol-3,20-dione.

IT 1099-19-0, 5 $\alpha$ -Pregnane-3,20-dione, 11 $\beta$ ,12 $\beta$ -epoxy-  
 1099-20-3, Pregn-4-ene-3,20-dione, 11 $\beta$ ,12 $\beta$ -epoxy- 1100-16-9,  
 5 $\beta$ -Pregnane-3,20-dione, 12 $\alpha$ -bromo-11 $\beta$ -hydroxy-  
 1104-14-9, 5 $\beta$ -Pregnan-20-one, 11 $\beta$ ,12 $\beta$ -epoxy-3 $\alpha$ ,21-  
 dihydroxy-, 21-acetate 1240-91-1, 5 $\beta$ -Pregnane-3,20-dione,  
 11 $\beta$ ,12 $\beta$ -epoxy- 1242-46-2, 5 $\beta$ -Pregnan-20-one,  
 12 $\alpha$ -bromo-3 $\alpha$ ,11 $\beta$ -dihydroxy- 1242-47-3,  
 Pregn-4-ene-3,20-dione, 12 $\alpha$ -bromo-11 $\beta$ -hydroxy- 1244-45-7,  
 5 $\beta$ -Pregnane-3,20-dione, 4 $\beta$ ,12 $\alpha$ -dibromo-11 $\beta$ -hydroxy-  
 1244-81-1, 5 $\beta$ -Pregnan-20-one, 12 $\alpha$ ,21-dibromo-3 $\alpha$ ,11 $\beta$ -  
 dihydroxy- 1249-88-3, 5 $\beta$ -Pregnane-3,20-dione, 11 $\beta$ ,12 $\beta$ -  
 epoxy-21-hydroxy-, acetate  
 (preparation of)

L25 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1963:448604 HCAPLUS

DN 59:48604

OREF 59:8825e-h,8826a-h,8827a-b

ED Entered STN: 22 Apr 2001

TI Reduction of 10-cyano- $\Delta$ 5-steroids by means of alkali metal solutions

AU Gardi, Rinaldo; Pedrali, Cesare; Ercoli, Alberto  
SO Gazzetta Chimica Italiana (1963), 93(5), 525-41  
CODEN: GCITA9; ISSN: 0016-5603  
DT Journal  
LA Unavailable  
CC 42 (Steroids)  
GI For diagram(s), see printed CA Issue.  
AB To a solution of 2.1 g. 10-cyano-19-nor-5-androstene-3 $\beta$ ,17 $\beta$ -diol (I) in 380 ml. Me<sub>2</sub>CO was added dropwise under N 5 ml. 8N chromic acid. After 5 min. stirring (under N) the mixture was poured into H<sub>2</sub>O and extracted with Et<sub>2</sub>O. From the Et<sub>2</sub>O exts. was obtained 1.35 g. 10-cyano-19-nor-5-androstene-3,17-dione (II), m. 152-6° (MeOH), [ $\alpha$ ]<sub>D</sub> -69°. To a solution of 840 mg. II in 75 ml. C<sub>6</sub>H<sub>6</sub> was added 3 ml. ethylene glycol containing 50 mg. p-toluenesulfonic acid. The mixture was refluxed overnight, and H<sub>2</sub>O separated from the reaction by a Marcussen separator. A few drops of pyridine was added and most of the C<sub>6</sub>H<sub>6</sub> was taken off in vacuo. The residue, taken up in MeOH, crystallized to give 785 mg. 10-cyano-19-nor-5-androstene-3,17-dione bis(ethylene ketal) (III), m. 211-12° (MeOH), [ $\alpha$ ]<sub>D</sub> -133° (dioxane). To a suspension of 10 g. Na in 150 ml. refluxing dry toluene was added a solution of 1.1 g. III in a mixture of 15 ml. EtOH and 15 ml. dry toluene, 40 ml. more dry EtOH added, the mixture cooled, the Na decomposed with EtOH, and the mixture diluted with H<sub>2</sub>O. The toluene was separated and the aqueous layer extracted with Et<sub>2</sub>O. From the combined organic exts. was obtained 1 g. gummy 3,3,17,17-bis(ethylenedioxy)-19-norandrostene [ $\Delta$ 5(10) +  $\Delta$ 5] (IV), [ $\alpha$ ]<sub>D</sub> 35°. Likewise a mixture of 7.2 g. 19-nor-4-androstene-3,17-dione (V), 500 mg. p-toluenesulfonic acid, and 30 ml. ethylene glycol in 560 ml. C<sub>6</sub>H<sub>6</sub> was treated as described for the preparation of III. Here 5.95 g. gummy IV was obtained. IV was also obtained by similarly preparing the diketal (VI) of 19-nor-5(10)-androstene-3,17-dione (VII,  $\Delta$ 5(10)). To a solution of 2 g. IV in 200 ml. Et<sub>2</sub>O was added 20 ml. 15% Et<sub>2</sub>O solution of monoperphthalic acid. The next day the Et<sub>2</sub>O was washed with NaHCO<sub>3</sub>, then H<sub>2</sub>O. A gum (1.99 g.) was obtained, which was taken up in C<sub>6</sub>H<sub>6</sub> and chromatographed (Florisil). From C<sub>6</sub>H<sub>6</sub>-Et<sub>2</sub>O (3:2) was obtained 1.3.5 g. crude material. Recrystns. from MeOH, then hexane, gave 5 $\beta$ ,10 $\beta$ -oxido-19-norandrostane-3,17-dione 3,17-bis(ethylene ketal) (VIIa), m. 116-17°, fold 10°. Evaporation of the MeOH liquors from the above and recrystn. (MeOH) gave 98 mg. 5 $\alpha$ ,10 $\alpha$ -oxido-19-norandrostane-3,17-dione 3,17-bis(ethylene ketal) (VIII), m. 120-1°, [ $\alpha$ ]<sub>D</sub> 20°. The last column elution (C<sub>6</sub>H<sub>6</sub>:Et<sub>2</sub>O, 1:1) gave 370 mg. 5 $\alpha$ ,6 $\alpha$ -oxido-19-norandrostane-3,17-dione 3,17-bis(ethylene ketal) (IX), m. 190-1° (MeOH), [ $\alpha$ ]<sub>D</sub> -41°. A solution of 500 mg. VIIa in 20 ml. 50% HOAc was left 15 hrs. at room temperature. After dilution in H<sub>2</sub>O and salting with NaCl, the mixture was extracted with CHCl<sub>3</sub>. From this extract was obtained 320 mg. 19-norandrostane-5 $\alpha$ ,10 $\beta$ -diol-3,17-dione (X), m. 240-1° (Me<sub>2</sub>CO-hexane), [ $\alpha$ ]<sub>D</sub> 97°. Likewise treatment of IX in the same manner gave X. A solution of 100 mg. X in 5 ml. Me<sub>2</sub>CO, treated with dilute HCl, was refluxed 20 min. After evaporation of solvent, the residue was taken up in Et<sub>2</sub>O. Repeated recrystns. (Me<sub>2</sub>CO-hexane) gave 19-nor-4-androsten-10 $\beta$ -ol-3,17-dione (XI), m. 206-7°, [ $\alpha$ ]<sub>D</sub> 148°. XI was also obtained by treating VIIa and VIII with dilute HCl. A solution of 100 mg. XI in 5 ml. Me<sub>2</sub>CO was refluxed 30 min. with concentrated HCl. Dilution with H<sub>2</sub>O gave 66 mg. estrone (XII), m. 250-3°, [ $\alpha$ ]<sub>D</sub> 163° (dioxane). To a suspension of 10 g. Na in 100 ml. dry boiling toluene was added 1.25 g. I, dissolved in 35 ml. absolute EtOH. The reaction was run as in the preparation of IV to give 1.05 g. 19-nor-androstene-3 $\beta$ ,17 $\beta$ -diol (mixture of isomers) (XIII), m. 148-51° (Me<sub>2</sub>CO), [ $\alpha$ ]<sub>D</sub> 73°. XIII (100 mg.) was treated with Ac<sub>2</sub>O in pyridine. The diacetate (XIV) formed, m. 82-4° (MeOH), [ $\alpha$ ]<sub>D</sub> 32°. A solution of 1.59 g. I in 30 ml. tetrahydrofuran and 30 ml. absolute EtOH was added dropwise to 300 ml. liquid NH<sub>3</sub>. Li was added portionwise to the persistence of a blue color and the mixture stirred until the blue disappeared. To this was added 50 ml. EtOH and most of the solvent removed. When the volume was approx. 100 ml., 200 ml. Et<sub>2</sub>O was added and the mixture heated to rid of NH<sub>3</sub>. After dilution with

H<sub>2</sub>O, and washing and drying the organic extract, evaporation gave 1.22 g. XIII, m. 148-50° (Me<sub>2</sub>CO), [α]<sub>D</sub> 55°. To a solution of 275 mg. of the diol mixture XIII in 75 ml. CHCl<sub>3</sub> was added 160 mg. Br in CHCl<sub>3</sub>. After evaporation of CHCl<sub>3</sub> the residue was dissolved in 15 ml. AcOH and treated overnight with 300 mg. CrO<sub>3</sub> in 3 ml. HOAc. This was poured into H<sub>2</sub>O, extracted with Et<sub>2</sub>O and the solid residue obtained was dissolved in 43 ml. EtOH and refluxed 3 hrs. with 600 mg. Zn. Removal of Zn and evaporation of EtOH gave a semi-oil residue mixture of VII. Recrystn. (MeOH-then aqueous MeOH) gave VII, m. 141-3°, [α]<sub>D</sub> 268°. A solution of 500 mg. XIII in 160 ml. Me<sub>2</sub>CO was oxidized with 8N CrO<sub>8</sub> (as in preparation of II). A residue (280 mg.) was worked up with Et<sub>2</sub>O to give 35 mg. VII [Δ<sub>5</sub>(10)], which on crystallization m. 142-4°, [α]<sub>D</sub> 268°.

To a solution of 500 mg. of the diol mixture XIII in 30 ml. toluene and 6 ml. cyclohexane was added 550 mg. Al(OPr-iso)<sub>3</sub> in 10 ml. dry toluene and the mixture refluxed 3 hrs. Addition of aqueous HCl caused separation of phases. The aqueous

phase was extracted with Et<sub>2</sub>O and the Et<sub>2</sub>O and toluene combined. After washing the combined organic phase with H<sub>2</sub>O, the mixture was steam distilled. The residue, extracted again with Et<sub>2</sub>O, gave 300 mg. oily mixture of V and 19-nor-5(10)-androstene-3,17-dione (VII, Δ<sub>5</sub>(10)). A solution of 100 mg. of the mixture VII, in 8 ml. MeOH was treated with 5 drops 2N KOH 15 min. under N. Evaporation in vacuo and dilution with H<sub>2</sub>O gave 72 mg. V, which on recrystn. (MeOH), m. 168-70°, [α]<sub>D</sub> 136°. To a solution of the ketal IV, obtained by reduction of 640 mg. III, in 40 ml. MeOH was added dilute HCl and the mixture refluxed 15 min. Dilution with H<sub>2</sub>O gave 266 mg. V, m. 168-70° (MeOH), [α]<sub>D</sub> 136°. One g.

10-cyano-19-nor-5-pregnene-3β,20β-diol (XV) was oxidized with CrO<sub>3</sub> (as in the preparation of II). Here 645 mg. 10-cyano-19-nor-5-pregnene-3,20-dione (XVI) was obtained, which on recrystn. (MeOH) m. 192-6°, [α]<sub>D</sub> -45°. Next 4 g. XVI was treated with ethylene glycol in C<sub>6</sub>H<sub>6</sub> and p-toluenesulfonic acid to give 3.95 g. 10-cyano-19-nor-5-pregnene-3,20-dione bis(ethylene ketal) (XVII), m. 209-10° (CH<sub>2</sub>Cl<sub>2</sub>MeOH), [α]<sub>D</sub> -82° (dioxane). A MeOH solution of 200 mg. XVII was heated 15 min. with a few drops dilute HCl to give 10-cyanonorprogesterone (XVIII), m. 159-61° (MeOH), [α]<sub>D</sub> 263°. From 1.1 g. XVII by

reduction with Na-EtOH in toluene, there was obtained 725 mg. 3,3,20-bis(ethylenedioxy)-19-nor-5(10)pregnene (XIX), m. 140-1°, [α]<sub>D</sub> 108° (dioxane). A solution of 900 mg. XVII in 20 ml. dry tetrahydrofuran and 200 ml. absolute EtOH was added to 200 ml. liquid NH<sub>3</sub>, then treated with Li (as in the preparation of XIII). This gave 609 mg. XIX, m. 140-1° (MeOH), [α]<sub>D</sub> 107°. 19-Norprogesterone (XX)

was treated with ethylene glycol in the usual manner to give 1.1 g. XIX, m. 137-8°, [α]<sub>D</sub> 108° (dioxane). To a solution of 250 mg.

XIX in 20 ml. Et<sub>2</sub>O was added 6 ml. 18% Et<sub>2</sub>O solution of monoperphthalic acid and the mixture left overnight. From the Et<sub>2</sub>O after workup was obtained 225 mg. 5β,10β-oxido-19-norpregnane-3,20-dione 3,20-bis(ethylene ketal) (XXI), m. 129-32°, chromatographed on Florisil. From the

C<sub>6</sub>H<sub>6</sub>-Et<sub>2</sub>O (3:2) eluate was obtained 205 mg. pure XXI, m. 136-7° (MeOH), [α]<sub>D</sub> 58°. Reduction of 1.25 g. XV with Na-EtOH in toluene gave 965 mg. 19-norpregnene-3β,20β-diol (mixture of isomers) (XXII), m. 160-2° (Me<sub>2</sub>CO), [α]<sub>D</sub> 70°. XXII

(200 mg.) was acetylated with Ac<sub>2</sub>O in pyridine to give 194 mg.

19-norpregnene-3β,20β-diol diacetate (XXIII), m. 108-10°

(MeOH), [α]<sub>D</sub> 74°. Reduction of 1.6 g. XV with Li-EtOH in NH<sub>3</sub> gave 1.35 g. of the mixture XXII, m. 159-62°, [α]<sub>D</sub> 68°.

XXII was oxidized as was XIII. From 900 mg. XXII after bromination, CrO<sub>3</sub> oxidation, and debromination with Zn, was obtained 305 mg. of a mixture of diones, m. 62-5°. After digestion in Et<sub>2</sub>O-petr. ether, 110 mg.

19-nor-5(10)-pregnene-3,20-dione (XXIV) was obtained which on recrystn.

(dilute MeOH) gave pure XXIV, m. 101-2°, [α]<sub>D</sub> 246°.

From the oxidation of 500 mg. XXII with 8N CrO<sub>3</sub> was obtained 290 mg. gum, which yielded (Et<sub>2</sub>O-petr. ether) 35 mg. XXIV, m. 98-101°.

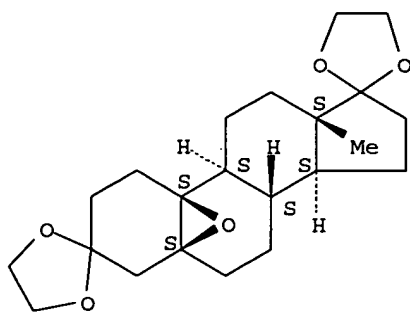
Oppenauer oxidation of 500 mg. XXII gave 285 mg. oily product, consisting of a mixture of 19-norpregnene-3,20-dione isomers. XXIV was also isolated following mild hydrolysis of XIX. A suspension of 100 mg. XIX in 8 ml.

50% HOAc was shaken and left overnight. After H<sub>2</sub>O dilution and Et<sub>2</sub>O extraction,

work up yielded an oil, which on treatment with aqueous MeOH gave 40 mg. XXIV, m. 101-2° (MeOH). A solution of 100 mg. XXIV was treated with 2N KOH to give 85 mg. XX, m. 144-5° (MeOH),  $[\alpha]_D^{25}$  147°. The diketal (XIX) (650 mg.) hydrolyzed by slight warming in MeOH-dilute HCl gave 430 mg. XX, m. 141-3°, which on recrystn. (MeOH) gave anal. pure XX identical with the product prepared by other methods.

- IT Spectra, visible and ultraviolet  
(of estr-4-ene-3,17-dione and congeners)
- IT Reduction  
Spectra, infrared  
(of  $\Delta^5$ -steroid 19-nitriles)
- IT Steroids  
( $\Delta^5$ -unsatd., 19-nitriles, reduction of)
- IT 19-Norpregn-5(10)-ene-3 $\beta$ ,20 $\beta$ -diol, diacetate, mixture with  $\Delta^5$  analog  
19-Norpregn-5(10)-ene-3 $\beta$ ,20 $\beta$ -diol, mixture with  $\Delta^5$  analog  
19-Norpregn-5-ene-3 $\beta$ ,20 $\beta$ -diol, diacetate, mixture with  $\Delta^5$ (10) analog  
19-Norpregn-5-ene-3 $\beta$ ,20 $\beta$ -diol, mixture with  $\Delta^5$ (10) analog  
5 $\alpha$ -Estrane-3,17-dione, 5,10-dihydroxy-  
5 $\alpha$ -Estrane-3,17-dione, 5,6 $\alpha$ -epoxy-, cyclic bis(ethylene acetal)  
Estr-5(10)-ene-3,17-dione, cyclic bis(ethylene acetal), mixture with  $\Delta^5$  analog  
Estr-5(10)-ene-3 $\beta$ ,17 $\beta$ -diol, diacetate, mixture with  $\Delta^5$  analog  
Estr-5(10)-ene-3 $\beta$ ,17 $\beta$ -diol, mixture with  $\Delta^5$  analog  
Estr-5-ene-3,17-dione, cyclic bis(ethylene acetal), mixture with  $\Delta^5$ (10) analog  
Estr-5-ene-3 $\beta$ ,17 $\beta$ -diol, diacetate, mixture with  $\Delta^5$ (10) analog  
Estr-5-ene-3 $\beta$ ,17 $\beta$ -diol, mixture with  $\Delta^5$ (10) analog
- IT 53-16-7, Estrone 472-54-8, 19-Norpregn-4-ene-3,20-dione 734-32-7,  
Estr-4-ene-3,17-dione 1038-51-3, 19-Norpregn-5(10)-ene-3,20-dione  
1624-60-8, 5 $\beta$ -Estrane-3,17-dione, 5,10-epoxy-, cyclic  
bis(ethylene acetal) 1624-72-2, 19-Nor-5 $\beta$ -pregnane-3,20-dione,  
5,10-epoxy-, cyclic bis(ethylene acetal) 3962-66-1, Estr-5(10)-ene-3,17-  
dione 5772-67-8, Androst-5-ene-19-nitrile, 3,17-dioxo-, cyclic  
bis(ethylene acetal) 95289-85-3, Pregn-4-ene-19-nitrile, 3,20-dioxo-  
95289-86-4, Pregn-5-ene-19-nitrile, 3,20-dioxo- 101298-83-3,  
19-Norpregn-5(10)-ene-3,20-dione, cyclic bis(ethylene acetal)  
102049-34-3, Pregn-5-ene-19-nitrile, 3,20-dioxo-, cyclic bis(ethylene  
acetal) 102490-33-5, 5 $\alpha$ ,10 $\alpha$ -Estrane-3,17-dione,  
5,10-epoxy-, cyclic bis(ethylene acetal)  
(preparation of)
- IT 166-68-7, Dispiro[1,3-dioxolane-2,3'(4'H)-[5,10]epoxy[17H]cyclopenta[a]phe  
nanthrene-17',2''-[1,3]dioxolane] 175-26-8, Dispiro[1,3-dioxolane-  
2,3'(4'H)-[5,6]epoxy[5H]cyclopenta[a]phenanthrene-17'(2'H),2''-  
[1,3]dioxolane] 187-08-6, Dispiro[1,3-dioxolane-2,3'-  
[3H]cyclopenta[a]phenanthrene-17'(2'H),2''-[1,3]dioxolane]  
(steroid derivs.)
- IT 1624-60-8, 5 $\beta$ -Estrane-3,17-dione, 5,10-epoxy-, cyclic  
bis(ethylene acetal) 102490-33-5, 5 $\alpha$ ,10 $\alpha$ -Estrane-  
3,17-dione, 5,10-epoxy-, cyclic bis(ethylene acetal)  
(preparation of)
- RN 1624-60-8 HCAPLUS
- CN Estrane-3,17-dione, 5,10-epoxy-, cyclic bis(1,2-ethanediyl acetal),  
(5 $\beta$ )-(9CI) (CA INDEX NAME)

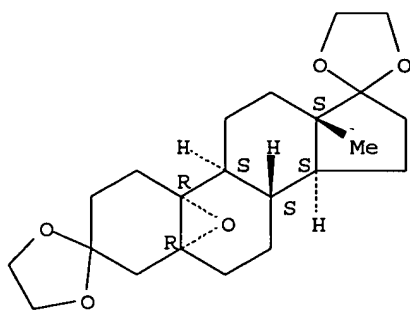
Absolute stereochemistry.



RN 102490-33-5 HCAPLUS

CN Estrane-3,17-dione, 5,10-epoxy-, cyclic bis(1,2-ethanediyl acetal),  
(5 $\alpha$ ,10 $\alpha$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L25 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1963:448603 HCAPLUS

DN 59:48603

OREF 59:8824g-h,8825a-e

ED Entered STN: 22 Apr 2001

TI Synthesis of pregnanediol derivatives. IV. Synthesis of  
Bhomo-5 $\alpha$ -pregnane-3 $\alpha$ ,20 $\alpha$ -diol

AU Himizu, Junichi

CS Tanabe Seiyaku Co., Saitama, Japan

SO Yakugaku Zasshi (1963), 83, 620-3

CODEN: YKKZAJ; ISSN: 0031-6903

DT Journal

LA Unavailable

CC 42 (Steroids)

AB cf. CA 59, 3985f. 3 $\beta$ -Acetoxycholestan-6-one (0.5 g.) in 10 ml. EtOH and 1 g. KCN at 0° treated dropwise with 2 ml. AcOH and the product extracted with Et<sub>2</sub>O gave the 6-cyanohydrin, oil, catalytic reduction of which in 10 ml. AcOH over 0.15 g. PtO<sub>2</sub> absorbed 2.3 moles H; the solution treated with 100 ml. H<sub>2</sub>O, kept overnight, the precipitate filtered off, the filtrate containing the 6-amino alc. acetate compound cooled; and this treated in H<sub>2</sub>O with HNO<sub>2</sub> gave 19 mg. 3 $\beta$ -acetoxy-B-homocholestan-7-one (I), m. 118-20°; semicarbazone m. 197° (decomposition); benzoate m. 152°. 3 $\beta$ -Acetoxycholestan-7-one (2 g.) in 20 ml. acetone cyanohydrin treated with 1 drop 10% NaOH, kept 10 min., H<sub>2</sub>O added, and the product filtered off gave 2.1 g. 7-cyanohydrin compound; catalytic reduction of this in 50 ml. AcOH over 0.3 g. PtO<sub>2</sub>, treating the solution with 150 ml. H<sub>2</sub>O containing 2 g. NaNO<sub>2</sub>, keeping overnight, and chromatographing the product (Al<sub>2</sub>O<sub>3</sub>) gave 0.7 g. I, m. 118-20°. Pregn-5-ene-3 $\beta$ ,20 $\alpha$ -diol diacetate (3.2 g.) in 15 ml. CCl<sub>4</sub>, 4 ml. Ac<sub>2</sub>O, and 8 ml. AcOH at 80° treated dropwise with CrO<sub>3</sub>-tert-BuOH (4 g. CrO<sub>3</sub>), the mixture stirred 9 hrs. at

Search done by Noble Jarrell

80°, cooled, poured into a cooled solution of 10 g. (CO<sub>2</sub>H)<sub>2</sub> in 500 ml. H<sub>2</sub>O, the whole kept overnight, and the product extracted with CHCl<sub>3</sub> gave 1.7 g. 3 $\beta$ ,20 $\alpha$ -diacetoxy-pregn-5-en-7-one (II), m. 163-4°, [ $\alpha$ ]<sub>D</sub><sup>24</sup> 121.4°. Catalytic reduction of 9 g. II in 100 ml. AcOEt over 5 g. 5% Pd-C gave 6.3 g. 3 $\beta$ ,20 $\alpha$ -diacetoxy-5 $\alpha$ -pregnan-7-one (III), m. 186-7° (MeOH), [ $\alpha$ ]<sub>D</sub><sup>24</sup> -46.2°. III (2 g.) in 60 ml. MeOH, 5 ml. H<sub>2</sub>O, and 0.3 g. K<sub>2</sub>CO<sub>3</sub> refluxed 30 min., cold H<sub>2</sub>O added, the product extracted with Et<sub>2</sub>O and chromatographed on Al<sub>2</sub>O<sub>3</sub> (3:7 hexane-C<sub>6</sub>H<sub>6</sub>) gave 1 g. 3 $\beta$ -hydroxy-20 $\alpha$ -acetoxy-5 $\alpha$ -pregnan-7-one (IV), m. 160-1.5°; IV and p-MeC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>Cl gave the 3 $\beta$ -tosyloxy analog of IV, m. 153-4°, [ $\alpha$ ]<sub>D</sub><sup>24</sup> -34.7°. A mixture of 1 g. above tosylate, 15 ml. AcOH, 3 ml. Ac<sub>2</sub>O, and 3 g. KOAc refluxed 3 hrs., the product extracted with Et<sub>2</sub>O and chromatographed on Al<sub>2</sub>O<sub>3</sub> in 7:3 hexane-C<sub>6</sub>H<sub>6</sub> gave 0.3 g. 20 $\alpha$ -acetoxy-5 $\alpha$ -pregnen-2(or 3)-en-7-one (V), and the 4:6 hexane-C<sub>6</sub>H<sub>6</sub> effluent gave 0.15 g. 3 $\alpha$ ,20 $\alpha$ -diacetoxy-5 $\alpha$ -pregnan-7-one (VI), m. 154° (MeOH). II (0.2 g.) in 15 ml. MeOH and 2.5 ml. concentrated HCl refluxed 3 hrs. and the product extracted with Et<sub>2</sub>O gave 20 $\alpha$ -acetoxy-pregna-3,5-dien-7-one (VII), m. 111-11.5°. Catalytic reduction of 30 mg. VII in 1.5 ml. AcOH over 10 mg. PtO<sub>2</sub> and keeping the product overnight in a mixture of 2 ml. 80% AcOH and 10 mg. CrO<sub>3</sub> gave 12 mg. 20 $\alpha$ -acetoxy-5 $\alpha$ -pregnan-7-one (VIII), m. 130-1°. Also, catalytic reduction of 0.3 g. VII in 7 ml. AcOH over 0.1 g. PtO<sub>2</sub> and oxidation of the product with AcOH-CrO<sub>3</sub> gave 1.6 g. VIII, m. 130-1°. VI (0.2 g.) in 3 ml. Me<sub>2</sub>CO cyanohydrin treated with 1 drop 10% NaOH, the mixture kept 10 min., H<sub>2</sub>O added, and the product extracted with Et<sub>2</sub>O gave an oily substance; catalytic reduction of this in 6 ml. AcOH over 30 mg. PtO<sub>2</sub>, treating the product with 25 ml. H<sub>2</sub>O, the solution at -5° treated with 0.2 g. NaNO<sub>2</sub> in 3 ml. H<sub>2</sub>O, kept overnight at room temperature, and the product filtered off and chromatographed (Al<sub>2</sub>O<sub>3</sub>) with hexane-C<sub>6</sub>H<sub>6</sub> gave 70 mg. 3 $\alpha$ ,20 $\alpha$ -diacetoxy-B-homo-5 $\alpha$ -pregnan-7-one (IX), m. 194-5° (MeOH). IX (50 mg.) in 2 ml. EtSH at 0° treated with 70 mg. ZnCl<sub>2</sub> and 150 mg. Na<sub>2</sub>SO<sub>4</sub>, kept 2 days at 5°, the EtSH removed in vacuo, the residue with H<sub>2</sub>O extracted with Et<sub>2</sub>O gave a thioketal, oil; catalytic reduction of this in dioxane over Raney Ni by heating 15 hrs. on a water bath and concentration of the solution gave 34 mg. of a diacetate, m. 138°, hydrolysis of which KOH-MeOH gave 25 mg. of B-homo-5 $\alpha$ -pregnane-3 $\alpha$ ,20 $\alpha$ -diol, m. 194-5°. III (0.5 g.) treated as in IX gave 0.18 g. 3 $\beta$ ,20 $\alpha$ -diacetoxy-B-homo-5 $\alpha$ -pregnan-7-one, m. 149-50° (Me<sub>2</sub>CO). Similarly, VIII gave 20 $\alpha$ -acetoxy-B-homo-5 $\alpha$ -pregnan-7-one, m. 132-4°.

IT Spectra, infrared

(of B-homo-5 $\alpha$ -pregnane-3 $\alpha$ ,20 $\alpha$ -diol and intermediates)

IT 26445-07-8, Pregnanediol

(derivs.)

IT 1612-79-9, B-Homo-5 $\alpha$ -pregnane-3 $\alpha$ ,20 $\alpha$ -diol 1624-76-6,  
 Pregn-5-en-7-one, 3 $\beta$ ,20 $\alpha$ -dihydroxy-, diacetate 1625-14-5,  
 5 $\alpha$ -Pregnan-7-one, 3 $\beta$ ,20 $\alpha$ -dihydroxy-, 20-acetate  
 3-p-toluenesulfonate 1805-05-6, B-Homo-5 $\alpha$ -pregnane-  
 3 $\alpha$ ,20 $\alpha$ -diol, diacetate 1805-20-5, 5 $\alpha$ -Pregnan-7-one,  
 3 $\beta$ ,20 $\alpha$ -dihydroxy-, diacetate 1805-21-6, 5 $\alpha$ -Pregnan-7-  
 one, 3 $\alpha$ ,20 $\alpha$ -dihydroxy-, diacetate 1969-99-9,  
 B-Homo-5 $\alpha$ -pregnan-7-one, 3 $\alpha$ ,20 $\alpha$ -dihydroxy-, diacetate  
 2319-65-5, 5 $\alpha$ -Pregnan-7-one, 3 $\beta$ ,20 $\alpha$ -dihydroxy-,  
 20-acetate 14652-41-6, B-Homo-5 $\alpha$ -cholestan-7-one,  
 3 $\beta$ -hydroxy-, acetate 94914-22-4, Androst-5-ene-19-nitrile,  
 3,17-dioxo- 95563-87-4, Pregna-3,5-dien-7-one, 20 $\alpha$ -hydroxy-,  
 acetate 95565-55-2, 5 $\alpha$ -Pregnan-7-one, 20 $\alpha$ -hydroxy-, acetate  
 96811-34-6, 5 $\alpha$ -Pregn-2-en-7-one, 20 $\alpha$ -hydroxy-(?), acetate  
 96811-36-8, 5 $\alpha$ -Pregn-3-en-7-one, 20 $\alpha$ -hydroxy-(?), acetate  
 101517-16-2, B-Homo-5 $\alpha$ -pregnan-7-one, 20 $\alpha$ -hydroxy-, acetate  
 103308-56-1, B-Homo-5 $\alpha$ -pregnan-7-one, 3 $\beta$ ,20 $\alpha$ -dihydroxy-,  
 diacetate 105819-25-8, B-Homo-5 $\alpha$ -cholestan-7-one,  
 3 $\beta$ -hydroxy-, benzoate 108042-16-6, B-Homo-5 $\alpha$ -cholestan-7-one,  
 3 $\beta$ -hydroxy-, semicarbazone, acetate  
 (preparation of)

=> b hcao

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L20 ANSWER 1 OF 3 HCAOLD COPYRIGHT 2005 ACS on STN

AN CA63:655g CAOLD

TI phenolic steroids and their ethers

AU Ercoli, Alberto; Gardi, R.; Pedrali, C.

PA Vismara, Francesco, Societa per Azioni

DT Patent

PATENT NO.	KIND	DATE
-----	-----	----
PI BE 641351		
DE 1223379		
FR 1394051		
NL 302028		
US 3231567		1966
IT 72-33-3	152-43-2	858-98-0
1624-60-8	1624-61-9	1624-62-0
1624-66-4	1624-67-5	1624-69-7
1624-74-4	1624-98-2	1667-98-7
102490-33-5		

L20 ANSWER 2 OF 3 HCAOLD COPYRIGHT 2005 ACS on STN

AN CA62:621c CAOLD

TI 19-norsteroids, particularly  $\Delta^5(10)$ -19-norsteroids oxygenated in the 6-position

PA CIBA Ltd.

DT Patent

PATENT NO.	KIND	DATE
-----	-----	----
PI FR 1369017		
GB 1011573		
NL 295431		
US 3178419		1965
IT 930-66-5	1091-89-0	1103-94-2
1246-95-3	1246-96-4	1249-35-0
1253-50-5		

L20 ANSWER 3 OF 3 HCAOLD COPYRIGHT 2005 ACS on STN

AN CA59:8825e CAOLD

TI reduction of 10-cyano- $\Delta^5$ -steroids by alkali metal solns.

AU Gardi, Rinaldo; Pedrali, C.; Ercoli, A.

Search done by Noble Jarrell



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IT  1038-51-3   1243-85-2   1624-60-8   1624-61-9   1624-72-2
    2220-74-8   3962-66-1   4993-32-2   5189-96-8   5772-67-8   14413-21-9
    21513-92-8   24428-62-4   25975-59-1   31321-37-6   94003-72-2   94914-22-4
    95289-85-3   95289-86-4   101298-82-2   101298-83-3   101517-16-2   102049-34-3
    102490-33-5   103004-85-9   103308-56-1

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=> b reg

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STRUCTURE FILE UPDATES: 26 JUN 2005 HIGHEST RN 852987-17-8

DICTIONARY FILE UPDATES: 26 JUN 2005 HIGHEST RN 852987-17-8

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TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

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*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*
*****

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Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d ide l28 tot

L28 ANSWER 1 OF 4 REGISTRY COPYRIGHT 2005 ACS on STN

RN 102490-33-5 REGISTRY

ED Entered STN: 31 May 1986

CN Estrane-3,17-dione, 5,10-epoxy-, cyclic bis(1,2-ethanediyl acetal), (5 $\alpha$ ,10 $\alpha$ )- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 5 $\alpha$ ,10 $\alpha$ -Estrane-3,17-dione, 5,10-epoxy-, cyclic bis(ethylene acetal) (7CI)

CN Dispiro[1,3-dioxolane-2,3' (4'H)-[5,10]epoxy[17H]cyclopenta[a]phenanthrene-17',2''-[1,3]dioxolane], estrane-3,17-dione deriv.

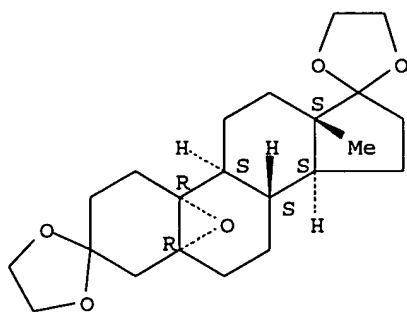
FS STEREOSEARCH

MF C22 H32 O5

SR CAOLD

LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS, CASREACT, TOXCENTER, USPATFULL (\*File contains numerically searchable property data)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

6 REFERENCES IN FILE CA (1907 TO DATE)  
6 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L28 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2005 ACS on STN

RN 1624-60-8 REGISTRY

ED Entered STN: 16 Nov 1984

CN Estrane-3,17-dione, 5,10-epoxy-, cyclic bis(1,2-ethanediyl acetal),  
(5β)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 5β-Estrane-3,17-dione, 5,10-epoxy-, cyclic bis(ethylene acetal) (7CI)

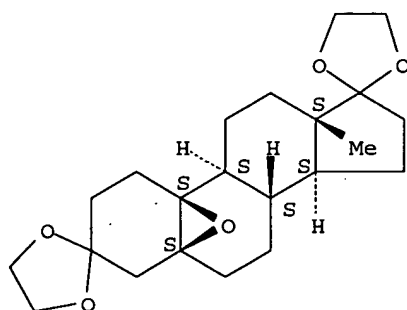
CN Dispiro[1,3-dioxolane-2,3' (4'H) - [5,10]epoxy[17H]cyclopenta[a]phenanthrene-  
17',2''-[1,3]dioxolane], estrane-3,17-dione deriv.

FS STEREOSEARCH

MF C22 H32 O5

LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS  
(\*File contains numerically searchable property data)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1907 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L28 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2005 ACS on STN

RN 1249-41-8 REGISTRY

ED Entered STN: 16 Nov 1984

CN Estrane-3,17-dione, 5,10-epoxy-6-hydroxy-, cyclic bis(1,2-ethanediyl  
acetal) (9CI) (CA INDEX NAME)

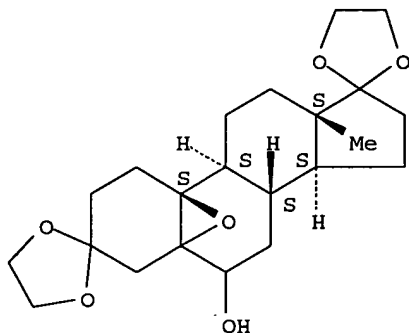
OTHER CA INDEX NAMES:

CN Dispiro[1,3-dioxolane-2,3' (4'H) - [5,10]epoxy[17H]cyclopenta[a]phenanthrene-

Search done by Noble Jarrell

17',2''-[1,3]dioxolane], estrane-3,17-dione deriv.  
 CN Estrane-3,17-dione, 5,10-epoxy-6-hydroxy-, cyclic bis(ethylene acetal)  
 (7CI, 8CI)  
 FS STEREOSEARCH  
 MF C22 H32 O6  
 LC STN Files: BEILSTEIN\*, CAOLD  
 (\*File contains numerically searchable property data)

Absolute stereochemistry.

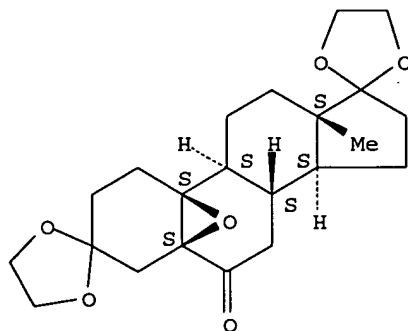


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L28 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2005 ACS on STN  
 RN 1103-94-2 REGISTRY  
 ED Entered STN: 16 Nov 1984  
 CN Estrane-3,6,17-trione, 5,10-epoxy-, cyclic 3,17-bis(1,2-ethanediyl  
 acetal), (5 $\beta$ )- (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN Dispiro[1,3-dioxolane-2,3' (4'H) - [5,10]epoxy[17H]cyclopenta[a]phenanthrene-  
 17',2''-[1,3]dioxolane], estrane-3,6,17-trione deriv.  
 CN Estrane-3,6,17-trione, 5,10-epoxy-, cyclic 3,17-bis(ethylene acetal) (7CI)  
 FS STEREOSEARCH  
 MF C22 H30 O6  
 LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS  
 (\*File contains numerically searchable property data)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1907 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

Search done by Noble Jarrell

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> b home

FILE 'HOME' ENTERED AT 08:29:11 ON 27 JUN 2005

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FILE 'CASREACT' ENTERED AT 08:29:48 ON 27 JUN 2005

L29 STR  
 L30 0 L29  
 L31 1 L29 FULL

=&gt; b casre

FILE 'CASREACT' ENTERED AT 08:39:05 ON 27 JUN 2005

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FILE CONTENT:1840 - 26 Jun 2005 VOL 142 ISS 26

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 \*  
 \* CASREACT now has more than 9.2 million reactions \*  
 \*  
 \*\*\*\*\*

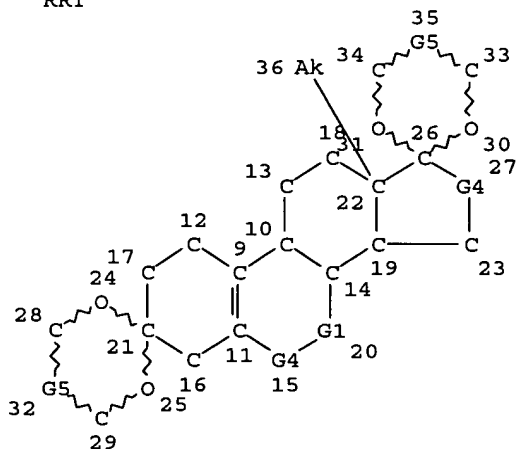
Some CASREACT records are derived from the ZIC/VINITI database (1974-1991) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

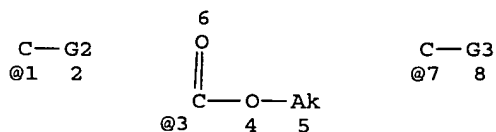
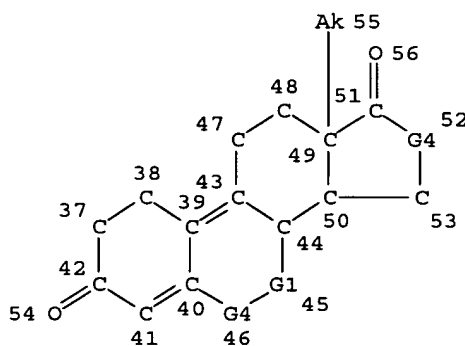
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L29 STR

RRT



PRO



VAR G1=C/1  
 VAR G2=AK/3  
 VAR G3=AK/O/X

Search done by Noble Jarrell

VAR G4=C/7  
 REP G5=(0-1) C  
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 DEFAULT MLEVEL IS ATOM  
 DEFAULT ELEVEL IS LIMITED

GRAPH ATTRIBUTES:  
 RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 56

STEREO ATTRIBUTES: NONE

L31 1 SEA FILE=CASREACT SSS FUL L29 ( 3 REACTIONS)

100.0% DONE 18 VERIFIED 3 HIT RXNS 1 DOCS  
 SEARCH TIME: 00.00.01

=> d bib abs crd retable l31 tot

L31 ANSWER 1 OF 1 CASREACT COPYRIGHT 2005 ACS on STN

AN 138:24878 CASREACT

TI Process for preparing estra-4,9(10)-diene-3,17-dione steroids from  
 19-nor-androst-4-ene-3-one steroids

IN Van Rheenen, Verlan H.; Hessler, Edward J.

PA Bridge Organics Co., USA

SO PCT Int. Appl., 23 pp.

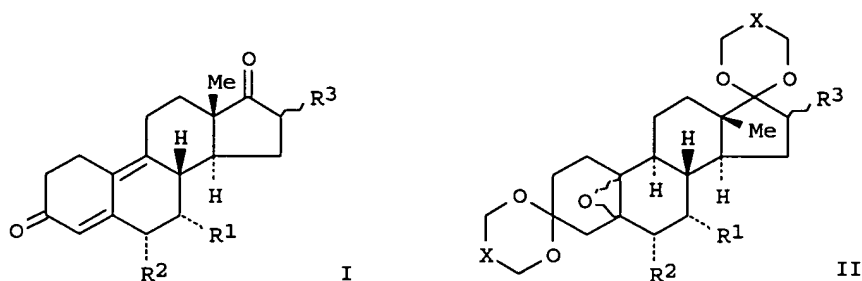
CODEN: PIXXD2

DT Patent

LA English

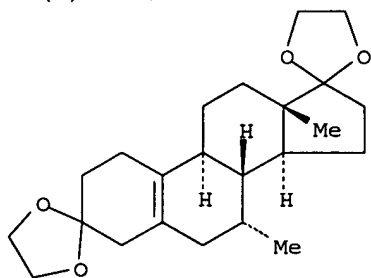
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002101014	A2	20021219	WO 2002-US18305	20020607
	WO 2002101014	A3	20040325		
	WO 2002101014	B1	20040506		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003004333	A1	20030102	US 2002-163727	20020606
	US 6812358	B2	20041102		
	US 2004087785	A1	20040506	US 2003-695122	20031028
PRAI	US 2001-296999P		20010608		
	US 2002-163727		20020606		
OS	MARPAT 138:24878				
GI					



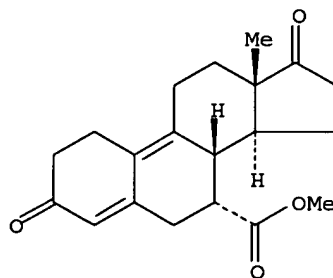
AB The present invention discloses a novel process for preparing estra-4,9(10)-diene-3,17-dione derivs. such as I [ $R_1 = \text{Me}, \text{H}, \text{CO}_2\text{Me}$ ;  $R_2 = \text{Me}, \text{F}, \text{H}$ ;  $R_3 = \text{Me}, \text{OH}, \text{F}, \text{H}$ ], from readily available 19-nor-androst-4-ene-3-one derivs. such as II [ $X = \text{bond}, \text{C}(\text{Me})_2, \text{CH}_2$ ], by a three-step process. Thus, epoxidn. of 7 $\alpha$ -methyl-estra-5(10)-ene-3,17-dione-3,17-bis-ethylene glycol ketal afforded 7 $\alpha$ -methyl-estra-5(10)-oxido-3,17-dione-3,17-bis-ethylene glycol ketal which upon treatment with hydrochloric acid provided 10-hydroxy-7 $\alpha$ -methyl-estra-4-ene-3,17-dione (III) and 5,10-dihydroxy-7 $\alpha$ -methyl-estra-4-ene-3,17-dione (IV). III and IV were reacted with concentrated sulfuric acid to afford estra-4,9(10)-diene-3,17-dione I [ $R_1 = \text{Me}$ ;  $R_2, R_3 = \text{H}$ ]. Products of this process are important intermediates in the preparation of biol. active substances.

RX(6) OF 17

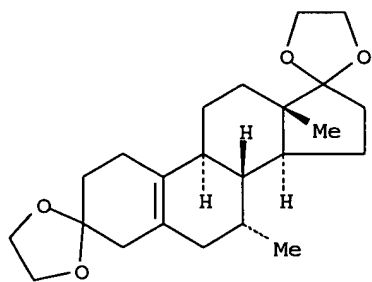


(step 1)

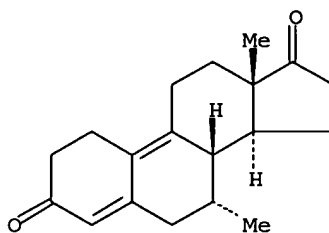
1.  $\text{K}_2\text{CO}_3$ , MCPBA,  $\text{CH}_2\text{Cl}_2$
2.  $\text{HCl}$ ,  $\text{Me}_2\text{CO}$ , Water
3.  $\text{K}_2\text{CO}_3$ , Water
4.  $\text{CH}_2\text{Cl}_2$ ,  $\text{H}_2\text{SO}_4$
5.  $\text{K}_2\text{CO}_3$ , Water



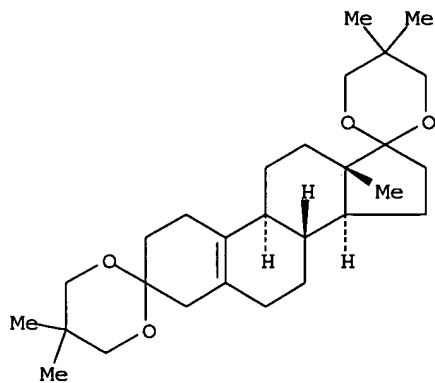
RX(16) OF 17 - 3 STEPS



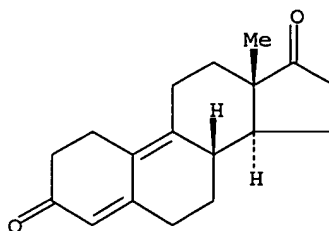
1. K<sub>2</sub>CO<sub>3</sub>, MCPBA, CH<sub>2</sub>Cl<sub>2</sub>
- 2.1. HCl, Me<sub>2</sub>CO, Water
- 2.2. K<sub>2</sub>CO<sub>3</sub>, Water
- 3.1. H<sub>2</sub>SO<sub>4</sub>, CH<sub>2</sub>Cl<sub>2</sub>
- 3.2. K<sub>2</sub>CO<sub>3</sub>, Water



RX(17) OF 17 - 3 STEPS



1. MCPBA, CH<sub>2</sub>Cl<sub>2</sub>
2. HCl, Me<sub>2</sub>CO, Water
3. H<sub>3</sub>PO<sub>4</sub>, H<sub>2</sub>SO<sub>4</sub>, Water, CH<sub>2</sub>Cl<sub>2</sub>



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